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THERAPEUTIC USES OF AN ARTIFICIAL KIDNEY.

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THE principle of the artificial kidney is extracorporeal dialysis, the patient's blood being made to pass outside the body over an artificial semi-permeable membrane, on the other side of which is a specially constituted watery solution. The constitution of the solution is so arranged as to encourage, through the concentration gradients, the diffusion of substances such as sodium, potassium, urea, etc. across the membrane, thus tending to correct the chemical abnormalities of the blood. Being only semi-permeable, the membrane does not allow large molecules like plasma proteins to pass.

Abel, Rowntree and Turner (1913) were the first to describe an apparatus of this type. They used it on dogs, and collodion tubes provided the semi-permeable membrane. However, it was not till 1943, when "Cellophane" was found to be a suitable membrane and heparin became available as an anticoagulant, that Kolff successfully used an artificial kidney clinically. The Kolff type of machine consisted essentially of a long length of "Cellophane" tubing wound spirally round a drum, which continuously rotated, immersing the tubing in a bath of fluid. Blood was pumped through the tubing. This machine, or modifications of it, has been extensively and successfully used, especially by Kolff (1947), Merrill (1952) and Hamburger and Richet (1956). Further modifications and other types of dialysers have been devised, with the object of reducing the over-all size, reducing the capacity of the "Cellophane" tubing, minimizing fluctuations in the volume of its contained blood, and eliminating moving parts from the machine. Alwall, in Sweden, designed an artificial kidney in 1946, which he has used very extensively (Alwall and Tornberg, 1953), and it is our experience with an Alwall type of apparatus[1] that we are reporting here.

Description and Operation of the Apparatus.

The essential part of the Alwall artificial kidney is a stainless steel cylindrical tank on wheels, containing 130 litres of bath fluid and a double cylinder of latticed stainless steel, between the two layers of which is housed the cellulose tubing. The "Perspex" lid of this dialyser carries an electric stirrer and a thermostatically controlled heater keeping the bath at 37° C. (Figure I). Arterial

[1] In receipt of a fellowship from the Adolf Basser Research Fund of The Royal Australasian College of Physicians.

[1] Given to Sydney Hospital by donations from Mr. and Mrs. F. D. Bonamy in memory of their daugter, Joan, and from the Anonymous Family Trust. Installation was completed by further donations from other supporters.

blood is forced by its own pressure through a glass cannula and the plastic tubing to the "Cellophane" tubing, as shown diagrammatically in Figure II. It flows through the 21·3 metres (70 feet) of "Cellophane" tubing, and returns to the patient by way of a bubble catcher, the plastic or rubber tubing and a cannula fixed into a vein. To prevent the blood clotting, the patient is given heavy doses of heparin. Blood flows at the rate of 200 ml. per minute, on the average, which means that the entire blood volume of the body passes through the machine every 30 minutes or so. In its passage through the cellulose tubing, which provides about 14,000 sq. cm. of surface area with pores of an average diameter of 24Å, dialysis occurs; substances such as urea, which are in high concentration in the blood, pass out into the fluid, while substances which are in higher concentration in the fluid, such as glucose, pass into the blood.

Figure I.
The Alwall-type artificial kidney in use at Sydney Hospital.

In the preparation of the machine for a course of treatment, the "Cellophane" tubing is sterilised by being boiled, and then wound round the spiral track of the inner latticed cylinder, and its ends are securely fixed to wide-bored plastic tubing. The outer lattice is slid over this assembly, and the whole immersed in water and the tubing tested for leaks by inflation with oxygen under pressure. If free of leaks, the tubing is flushed through with two or three litres of sterile saline solution, and then filled with heparinized blood freshly collected from donors (about 1500 ml.). The apparatus is then immediately connected to the patient, the arterial and venous cannulæ having previously been inserted under local anæsthesia, usually in the arm.

The dialysing solution is usually made up in the large 750 litre storage tank housed in the adjoining preparation room, and connected by pipes to the dialyser in the treatment room. Some of the elements, such as potassium, are added to the dialyser itself, so that the final composition can be varied according to the condition of the patient. The usual composition of the fluid used for our early anuric patients was sodium 130, potassium 4, calcium 5, magnesium 1, chlorine 100, carbonic acid 30 mEq/l., and glucose 1500 mg. per 100 ml. The total osmolarity of this fluid was slightly higher than that of normal plasma. Latterly we have sometimes reduced the glucose to 150 mg. per 100 ml. Carbon dioxide, 5% in oxygen, is bubbled continuously through the solution. The fluid in the dialyser can be evacuated rapidly by pumping, and a fresh supply run in by gravity from the storage tank. This was usually done at two-hourly intervals.

During the course of treatment, a nurse, a doctor and a technician were in constant attendance. The blood pressure, pulse rate, body temperature, bath temperature and blood flow were checked frequently, and measurements of hæmoglobin value, coagulation time and serum electrolytes were made at regular intervals. Heparin remaining at the end of dialysis was counteracted by an injection of protamine sulphate.

The Effectiveness of Dialysis.

The artificial kidney finds its greatest use in the treatment of acute oliguric renal failure. The benefits from treatment are most marked in patients suffering from

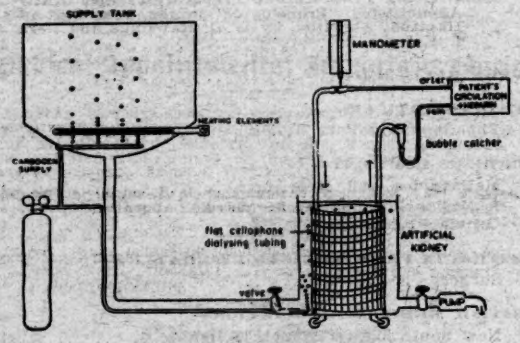

Figure II.
Diagram showing the patient's extracorporeal circulation, and the artificial kidney and its ancillary equipment.

the symptoms and signs of severe uræmia or from disturbances of water, electrolyte or acid-base balance. The apparatus can also remove from the patient's blood certain drugs such as streptomycin, phenobarbitone, barbitone, bromides and salicylates. These are normally excreted by the kidneys, and are therefore liable to be retained and cause toxicity if given during acute or chronic renal failure.

These biochemical defects are generally reduced or even corrected by a single dialysis of five to ten hours' duration, and the patient's clinical condition may improve dramatically. Instead of being drowsy, confused, nauseated and vomiting, with muscular weakness and uræmic twitching, the patient may become fully conscious after dialysis, and within 24 hours have regained appetite and muscular strength and be able to sit out of bed. When dialysis is judiciously used, intravenous and intragastric tubes are rarely necessary, nursing is simplified and there is less likelihood of complications such as bed sores, bronchopneumonia and thrombo-embolism.

Some of the effects of dialysis observed among the 12 patients treated in this way up to June, 1958, are shown in Tables I and II, and considered in more detail below.[1]

Uræmia and Acidosis.

Patients who have had oliguric renal failure for several days commonly show signs of severe uræmia, with mental confusion or coma, acidotic breathing, muscular twitching,

[1] Up to March, 1959, dialysis has been used on 44 occasions in 31 patients.

TABLE I.

Clinical Details of Patients with Acute Renal Failure, whose Treatment Included Dialysis.

Case Number.	Patients' Ages. (Years.)	Diagnosis.	Indications for Dialysis.	Dialysis (Days After Onset).	Total Duration of Oliguria. (Days). (<1000 ml. per Day.)	Outcome.
I	50	Chronic renal failure, coma due to barbitone poisoning, broncho-pneumonia.	Barbitone.	2	—	Recovery, no sequelæ.
II	71	Chronic renal failure due to carcinoma of bladder and pyelonephritis.	Uræmia, hyperkalæmia.	?	—	Died 15 days after dialysis.
III	55	Traumatic amputation, mismatched blood transfusion, acute renal failure.	Uræmia, hyperkalæmia.	17	19	Recovery, no sequelæ.
IV	51	Diabetes mellitus, laminectomy, mismatched blood transfusion, acute renal failure, streptomycin poisoning.	Uræmia.	11	13	Recovery, residual vestibular damage causing disabling loss of balance.
V	28	Reactive depression, bullet wound, thoracotomy and shock, acute renal failure, streptomycin poisoning.	Uræmia.	15	16	Recovery, vestibular damage.
VI	38	Septic miscarriage (*B. welchii*), acute renal failure, streptomycin poisoning.	Streptomycin.	5	16	Recovery, no sequelæ.
VII	53	Transurethral prostatectomy, acute renal failure, generalized infection (pyæmic kidneys, broncho-pneumonia, purulent pericarditis).	Uræmia, acidosis, hyperkalæmia.	13, 19	21	Death from staphylococcal septicæmia.
VIII	30	Hypertension during pregnancy, ante-partum hæmorrhage, acute renal failure, streptomycin poisoning.	Overhydration, pulmonary œdema, streptomycin.	12	13	Recovery, persistent proteinuria.
IX	38	Septic miscarriage (*B. welchii*), acute renal failure, streptomycin poisoning.	Hyperkalæmia, streptomycin.	12	18	Recovery, some loss of balance for two months afterwards.
X	52	Cholecystectomy, myocardial infarction, acute renal failure due to massive renal infarction, left renal vein thrombosis, hepatic, splenic and cerebral embolism.	Hyperkalæmia, uræmia.	7	10	Died 26 days after onset.
XI	62	Prostatectomy, obstructive uropathy, pyelostomy, streptomycin poisoning.	Hyperkalæmia, streptomycin, preparation for operation.	8	11	Recovery, no sequelæ.
XII	8	Acute glomerulonephritis, brief anuria followed by oliguria.	Uræmic pericarditis and congestive failure, uræmia and acidosis, uræmia and congestive failure.	24, 71, 83	88+	Still in the oliguric phase.

nausea and vomiting. They become increasingly helpless, and present difficult problems in nursing and medical management. This state is due to some biochemical disorder, which can be relieved completely by dialysis, though no single cause has yet been ascertained. Three of the biochemical tests done here indicate the severity of uræmia. Plasma levels of creatinine and urea rise as the illness progresses, and uræmia is severe when they exceed 20 to 25 mg. per 100 ml. and 300 to 400 mg. per 100 ml. respectively. The plasma bicarbonate level falls in relation to increasing metabolic acidosis, and in severe uræmia is less than 10 mEq/l., with acidotic Kussmaul breathing apparent clinically. The effectiveness of hæmodialysis in uræmia is illustrated by the following experiences.

CASE III.—A man, aged 55 years, had an accident at work. Surgical amputation of his right leg was necessary, and during the operation he was shocked and received a transfusion of mismatched blood. Acute oliguric renal failure ensued. Hyperkalæmia developed and was partly controlled by "Resonium-A" given orally. After 17 days he was transferred to the Clinical Research Unit, Sydney Hospital. He was at first confused, and then became semi-comatose, with marked generalized twitching and with vomiting, and he could eat nothing in spite of chlorpromazine given by injection. Hyperkalæmia, intermittent pericardial friction rub, fever, tachycardia and gallop rhythm were present. He was treated by hæmodialysis at this stage, with the resulting biochemical changes shown in Table II and in Figure III. He became conscious during dialysis, his breathing became normal, and by the next day he was sitting out of bed, smoking cigarettes with enjoyment, and eating a diet of 1300 Calories. Muscular twitching and gallop rhythm disappeared two days after dialysis. Urine output began to increase from the time of dialysis, and full diuresis was established two days later. A small blood transfusion was given and he was discharged from hospital two weeks after the onset of diuresis, when all results to biochemical tests were normal.

CASE VII.—A man, aged 53 years, had had urgency and frequency of micturition, with a poor stream of urine, for four years. Transurethral prostatectomy was performed, with the use of tap water under pressure to distend the bladder. The same day he became jaundiced and ill, with pain in both loins and had acute oliguric renal failure. After five days he was transferred to the Clinical Research Unit, Sydney Hospital. Two days later he had a secondary hæmorrhage from the prostatic bed, requiring meatotomy and operative removal of the blood clot, and subsequent lavage of the bladder at frequent intervals. He developed hyperkalæmia controlled by "Resonium-A" given orally, and bronchopneumonia for which he was given penicillin. After 12 days, as he was drowsy and confused, with acidotic breathing, anorexia and muscular twitching, he was dialysed for five hours. All symptoms were relieved by the next day, except his breathlessness. He was still febrile and developed pustules on the skin, infection of his meatotomy wound and signs of consolidation of the lower lobe of the right lung. *Staphylococcus pyogenes* was cultured, which was sensitive to chloramphenicol, and a course of this antibiotic was given parenterally. Three days after dialysis, a harsh pericardial friction

TABLE II.

Effects of Dialysis on Biochemical Tests in Cases of Acute Renal Failure.

Case Number.	Before or After Dialysis.	Plasma Creatinine. (Mg. per 100 ml.)	Plasma Urea. (Mg. per 100 ml.)	Plasma (mEq/l.).					Plasma Calcium. (Mg. per 100 ml.)	Body Weight. (Kg.)	Duration of Dialysis. (Hours.)
				HCO_3	K	Na	Cl	SO_4[2]			
III	Before	34·3	385	10	7·2	129	87	23	7·6	—	10·0
	After	15·1	160	21	4·1	141	100	8	10·2	—	
IV	Before	18·9	320	17	3·8	123	81	13	—	—	10·0
	After	9·5	145	26	3·5	138	95	5	—	—	
V	Before	29·5	470	13	5·7	136	86	27	—	74·0	10·0
	After	15·0	235	23	4·2	134	95	4	—	70·0	
VI	Before	14·1	220	14	4·3	127	103	0	—	78·9	10·0
	After	7·4	140	23	3·9	129	96	0	—	75·9	
VIIa	Before	22·3	485	6	5·2	129	78	34	5·4	81·8	5·0
	After	14·4	285	16	3·7	129	87	14	7·4	79·0	
VIIb	Before	24·8	535	4	7·0	134	88	33	8·0	75·5	10·0
	After	11·2	215	18	4·3	134	98	6	9·0	—	
VIII	Before	19·4	355	7	6·2	129	89	23	—	56·0	10·0
	After	9·2	120	19	4·2	127	99	0	8·8	52·3	
IX	Before	16·4	525	12	7·9	129	89	20	—	—	4·0
	After	11·6	370	17	5·0	131	92	11	—	—	
X	Before	23·0[1]	395	10	6·4	125	83	22	—	—	8·0
	After	14·3	225	17	4·3	134	91	14	10·0	—	
XI	Before	—	320	8	7·7	121	90	15	8·5	53·6	9·0
	After	—	135	20	4·9	123	96	0	—	51·5	
XIIa	Before	17·4[1]	555	10	8·2	125	94	8	10·0	21·4	7·0
	After	7·7	215	19	2·8	136	98	6	10·0	21·2	
XIIb	Before	9·7	470	5	5·5	142	110	17	8·6	22·3	5·5
	After	6·3	285	15	4·4	132	98	7	9·5	21·2	

[1] The plasma level of creatinine was raised prior to dialysis by the injection experimentally of 5% creatinine.

[2] Unmeasured anions (SO_4, PO_4 and organic acid anions) were calculated rather inaccurately as described.

rub appeared, together with electrocardiographic changes of pericarditis, thought to be infective in origin. There was a slight increase in urine flow for a few days, but this then decreased again. After 18 days he was very ill, with generalized infection, and there were signs of severe uræmia and hyperkalæmia. Antibiotics were continued, and he was dialysed again for 10 hours. Biochemically there was marked improvement, as seen in Table II and in Figure IV, but clinically he remained very ill, with fever, mental confusion, vomiting and dyspnœa as before. Severe oliguria persisted and he died three days later, after 21 days of oliguria. Autopsy showed acute ascending pyelonephritis, causing pyæmic kidneys, purulent pericarditis, bronchopneumonia and pulmonary infarction. All these were in addition to acute oliguric renal failure due to acute tubular necrosis, which had followed the entry of tap water into the veins in the prostatic bed.

These two cases show that the clinical picture of uræmia can be completely relieved by dialysis. It is apparent from the second case that the persistence of any distressful symptoms after dialysis may be due to causes other than uræmia. Cases VIII, XI and XII, described later, also illustrate the response to dialysis of patients with severe uræmia.

High levels of creatinine and urea in the plasma, although probably not dangerous in themselves, serve as indicators of the severity of uræmia and of the accumulation of other solutes not measured here. Among these are sulphate ions and magnesium ions, which may play a part in causing the symptoms of uræmia (Hamburger and Richet, 1956). In uræmic acidosis, an excess of measured cations (sodium, potassium) over anions (bicarbonate, chloride and protein) reveals an appreciable level of unmeasured anions; the majority of these anions are sulphate and phosphate. If phosphate is assumed to balance calcium and magnesium, and protein is assumed to be present at a constant level in the plasma of 16 mEq/l, then the figures for sulphate shown in Table II are obtained. It can be seen that dialysis is effective in substantially lowering the high levels seen here.

Measurements of creatinine and urea in the blood entering and leaving the artificial kidney and in the dialysing solution at the end of each period allow of estimates being made of the effective blood flow through the machine and also of the relative efficiency with which it performs its function. With the use of this method, the blood flow through our machine has been found to vary from 130 to 300 ml. per minute, and the creatinine clearance from 60 to 110 ml. per minute. When only half the usual length of "Cellophane" dialysing membrane was wound on the cylinder, the clearance was 25 to 29 ml. per minute. This was sufficient for children, as shown later by Case V. The absolute fall in creatinine or urea levels is greatest initially, when plasma levels are high. However, the level at the end of any one hour of dialysis is on the average 92% of the level at the beginning of that hour. Thus the fall in creatinine level with time is logarithmic. Case III is representative, and the fall of plasma creatinine content during dialysis is shown in Figure V.

Hyperkalæmia.

If the plasma potassium level is raised, dialysis can lower it to normal within two to four hours.

CASE IX.—A woman, aged 38 years, had a septic miscarriage after 12 weeks of pregnancy. She became very ill, with fever, jaundice and anuria. Two days later she was admitted to hospital for curettage. *Bacillus welchii* was cultured from the placental debris. During the oliguric phase she received large doses of penicillin and a total of 10 grammes of streptomycin by injection. After 10 days she was transferred to the Clinical Research Unit, Sydney Hospital. On examination she was pale and jaundiced, mentally confused and restless. She had a toxic purpura over her abdomen and chest; her abdomen was distended and occasional bowel sounds were present; she had generalized muscular tenderness, twitching and marked weakness, with poor tone and coordination and diminished reflexes. An electrocardiogram showed high peaked *T* waves typical of hyperkalæmia. She was treated by hæmodialysis, but this was stopped after only four hours because of technical troubles. This short period of dialysis caused biochemical improvement, as shown in Table II, although this was not as marked and not as long-lasting as that resulting from dialysis for periods of 10 hours. She improved clinically with clearing of the uræmic symptoms, but mental confusion was replaced by an argumentative and suspicious attitude of mind. Hyperkalæmia recurred, but was controlled by "Resonium-A", and diuresis

commenced six days after dialysis. She had a stormy convalescence, with infections, severe anæmia and a paranoid mental state, together with gross muscular twitching, hyperexcitability and hyperreflexia. Magnesium deficiency was suspected; marked improvement occurred 24 hours after she was given magnesium parenterally, and improvement was complete in 48 hours. However, serum magnesium levels were not measured. She was discharged from hospital after nine weeks, free of symptoms and able to walk and balance normally. When she was seen again one month later, though well and managing to do her housework, she complained of vertigo and momentary blurring of vision if she moved her head suddenly. She had lost her balance several times while shopping and had fallen to the ground twice. This occurred if she attempted to turn round quickly, and she had modified her gait accordingly. These disturbances were attributed to delayed streptomycin poisoning. Three months later balance and caloric tests gave normal findings.

In addition to Case IX, the effect of dialysis on hyperkalæmia in other cases is shown in Table II. In Cases III, V, VIIb, VIII, IX, X and XI, plasma potassium levels

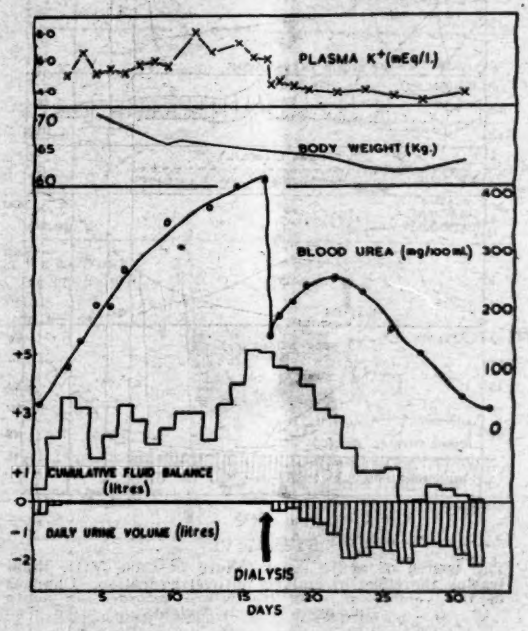

FIGURE III.
The course of acute renal failure in Case III, showing changes in the concentration of urea in the blood.

were raised above the normal range of four to five mEq/l., and were corrected by dialysis. All showed initially the characteristic electrocardiographic evidence—tall, spiked *T* waves—of hyperkalæmia, which reverted to normal after dialysis. Hyperkalæmia can cause death: our results emphasize the effectiveness of the artificial kidney, and suggest that emergency dialysis should be considered in any patient with a plasma potassium level higher than 7 mEq/l.

Overhydration.

The body weight is the simplest and most accurate measure of hydration in patients with acute renal failure. If the body fluids are to remain normal in volume, then body weight in adults should fall about 0·3 kg. per day during the oliguric phase, which allows for the catabolism of about 300 grammes of endogenous fat and protein. This means a daily fluid intake of only about 400 ml. If the daily weighing and control of fluid intake are neglected, the patient easily becomes overhydrated, often by as much as 10 litres. Congestive cardiac failure or pulmonary œdema can appear. These are refractory to all the usual methods of treatment, which rely on good renal function for their effectiveness. Even if the patient's intake of fluid is restricted to nil, overhydration takes several days to be relieved. If the situation is urgent, an effective way of removing water is by dialysis. Hypertonic dialysing solutions with or without a method of ultrafiltration can be used. In the same way that water is retained, salt given during the oliguric phase is also retained, and tends to aggravate overhydration by holding the excess water in the extracellular fluid compartment. A rising blood pressure is commonly found in acute renal failure, and is possibly related to retention of excess water and salt.

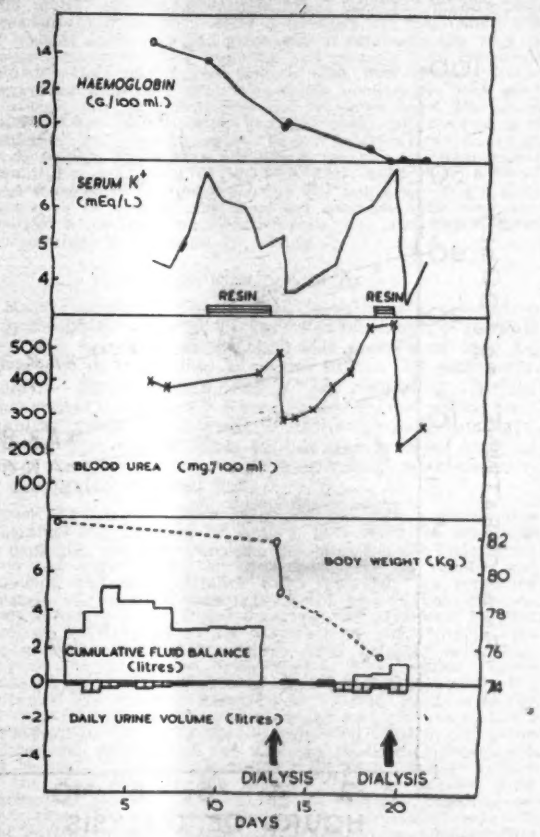

FIGURE IV.
The course of acute renal failure in Case VII, showing the effect of dialysis on hyperkalæmia.

CASE VIII.—A woman, aged 30 years, had been pregnant for 20 weeks. She was a primipara who had gained excessive weight, and her blood pressure had been 160/85 millimetres of mercury. A severe ante-partum hæmorrhage necessitated a Cæsarean section and a blood transfusion to correct shock. Acute oliguric renal failure followed. She was given penicillin and a total of 1·5 grammes of streptomycin during the oliguric phase, as well as several transfusions of whole blood in an attempt to correct anæmia. Her usual weight was 49 kilograms. After 10 days of anuria this should have been 46 kilograms, but instead she weighed 56 kilograms. She developed repeated attacks of breathlessness and cyanosis and was transferred to the Clinical Research Unit, Sydney Hospital. On examination she was pale, drowsy and breathless, but could answer questions. Her lips and tongue were slightly cyanosed, sore, dry and cracked. This latter finding resembled the dry, cracked tongue more frequently seen in patients thought to be dehydrated. She had a tachycardia of 120 beats per minute, a blood pressure of 190/115 millimetres of mercury, pitting œdema of the sacral region and gallop rhythm. Respirations were rapid and shallow, with moist crepitations over the lower lobes of both lungs and signs of pleural effusion. Acute streptomycin toxicity was suggested by vertigo, which occurred when she moved her

head or eyes suddenly to either side. Just before dialysis she knew she was going to die, but she felt far too weary to make any effort to help herself. She also felt quite remote from all the activity around her, and quite peaceful. Dialysis was commenced, and within four hours she had lost her pulmonary œdema and was sitting up in bed; she was mentally clear, talking normally and breathing easily. Dialysis was completed after 10 hours, and reweighing showed she had lost 3·7 kilograms. These changes in fluid balance are shown in Figure VI, and biochemical changes are recorded in Table II. Diuresis began the next day and she had a rapid and uneventful recovery. She was well enough to go home five weeks after the onset of her illness and had no evidence of streptomycin toxicity. Caloric tests of vestibular function gave normal results.

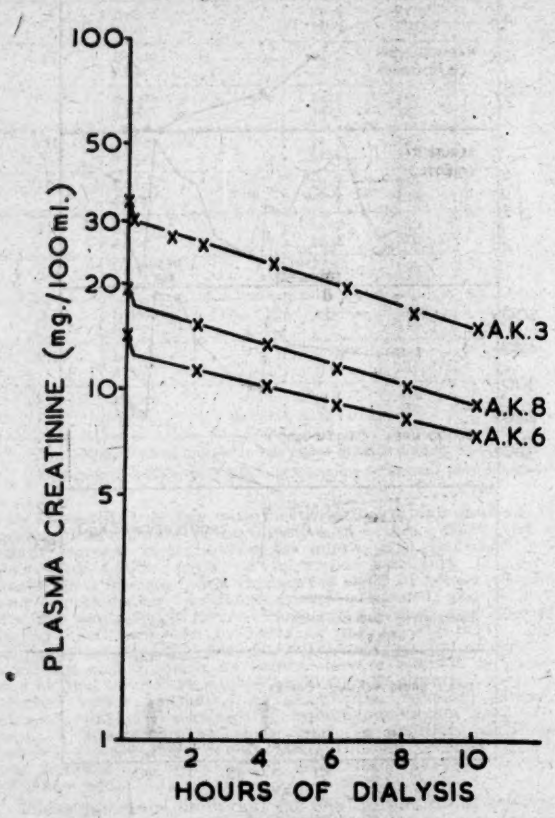

FIGURE V.

The change in the concentration of creatinine in plasma effected during dialysis.

CASE XII.—A girl, aged eight years, became anuric with acute glomerulonephritis. After five days she was transferred to the Clinical Research Unit, Sydney Hospital, where conservative management of her acute oliguric renal failure was begun, and it was maintained throughout the extremely long period of oliguria which ensued. After 16 days she began to vomit and had severe epigastric pain. Acute pericarditis with effusion developed, and by the twenty-fourth day of oliguria she was extremely ill, with vomiting, fever, a raised venous pressure and mild hypertension. She was dialysed for seven hours, with the use of 35 feet instead of the full quota of 70 feet of cellulose tubing in the artificial kidney. Mild hypokalæmia, probably due to previous treatment with "Resonium-A" and to vomiting, was aggravated during dialysis, even though the level of potassium in the dialysing solution was raised to 5·6 mEq/l. (see Table II). The patient was much improved, vomiting ceased and her appetite returned. One week after dialysis, all evidence of pericarditis had disappeared and she was able to sit out of bed. She talked happily to those attending her and was a good patient. Her oliguria continued, with an average output of 250 millilitres of urine per day. She settled into a steady phase, without much rise in the levels of urea or creatinine in the plasma. Her weight gradually increased. This was at first thought to be due to repair of tissue protein and fat stores, but measurements of her total body water showed that this was increasing at the same rate as her body weight. After 65 days of oliguria, the plasma creatinine and urea levels began to rise more rapidly, anæmia became worse, and she developed pitting œdema and a raised venous pressure. After 71 days she was very ill and had a grossly raised venous pressure and some hypertension. She was dialysed for the second time. After five and a half hours of dialysis, she had an epileptiform fit, so the treatment was discontinued. She lost 1·1 litres of water and some sodium and chloride during this dialysis, as shown by the alteration in body weight and in the plasma levels (Table II). The dialysis differed from others in having a low concentration of sodium and chloride ions in the dialysing solution. Thus the convulsion could possibly be explained by a sudden increase in intracellular water caused by the too rapid lowering of the patient's extracellular levels of sodium and chloride. The next day she was much improved, with a fall in venous congestion, a normal blood pressure and biochemical

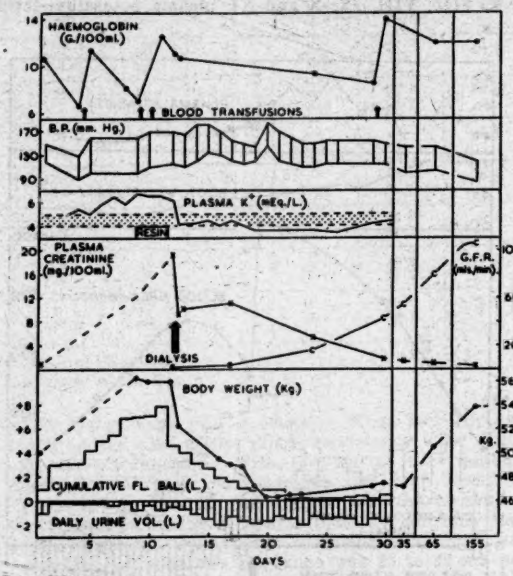

FIGURE VI.

The course of acute renal failure in Case VIII, illustrating the effect of dialysis on over-hydration. Changes in the volume of body water are recorded as acute changes in body weight.

improvement. Oliguria continued and was uninfluenced by a short course of prednisolone in high dosage. A percutaneous renal biopsy was unsuccessful. It was decided to maintain the patient alive as long as possible by repeated dialysis, as some patients with anuria due to acute nephritis have recovered after prolonged oliguria (Alwall, 1957). At the time of writing she has been oliguric for 88 days and has had three dialyses.

These two cases serve to illustrate the usefulness of the Alwall artificial kidney in the treatment of an excess of water and salt. The alteration in body weights of other patients after dialysis confirms that a loss of up to four litres of water can be obtained. The relative efficiency of osmotic forces and ultrafiltration is still being investigated. However, it is possible to encourage ultrafiltration by constriction of the outflow tube and the use of a mechanical pump on the inflow side of the circuit to raise the pressure of blood within the "Cellophane" tubing to 40 to 100 mm. of mercury We have found that water can be lost through ultrafiltration even when the osmolarity of the dialysing fluid is equal to, or even less than, the osmolarity of the patient's plasma.

Poisons.

Any drug which relies on intact kidney function for its excretion is potentially dangerous when administered to patients with renal failure. It accumulates, and is liable to produce any toxic effects it possesses.

CASE IV.—A man, aged 51 years, had been receiving treatment for diabetes mellitus for two months. He then had an operation for the removal of a herniated intervertebral disk and received 100 millilitres of mismatched blood by transfusion. Acute oliguric renal failure developed (Figure VII). He was given penicillin and streptomycin injections as a routine prophylactic measure after the operation. He received a total dose of six grammes of streptomycin before being transferred to the Clinical Research Department, Sydney Hospital. On the eleventh day of oliguria he was dialysed because of general symptoms of uræmia. After this procedure he began to pass urine and the diuretic phase proceeded without complication for two weeks. He then noticed giddiness on moving his head, eyes or arms and had difficulty in walking. He had complete loss of balance in the dark or with his eyes shut. Caloric tests showed bilateral loss of vestibular function. Renal function returned to

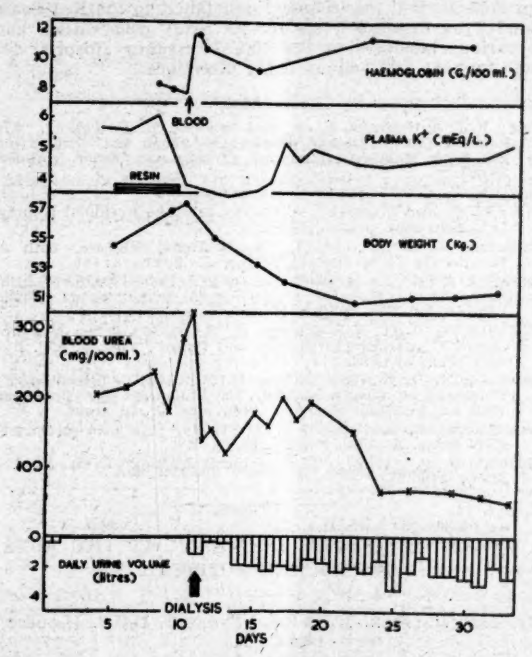

FIGURE VII.
The course of acute renal failure in Case IV.

normal, and the diabetes was later controlled by diet, but his loss of balance appeared to be permanent. Although he learned to balance aided by vision, he was greatly limited in his mobility, and was unable to return to any useful employment.

This case illustrates the toxic effects of streptomycin given during acute renal failure. Since treating this patient, we have shown that early dialysis can prevent the delayed toxic effects of the drug. Acute symptoms of toxicity developed in one oliguric patient after as few as three injections each of half a gramme of streptomycin. We have also confirmed, by in-vitro tests, that streptomycin can be removed from blood by dialysis, and five subsequent patients loaded with streptomycin have been treated by early dialysis. They have developed little or no vestibular damage (Edwards and Whyte, 1958). Cases VIII, IX and XI are representative.

Other poisons which can be removed by dialysis include bromides, salicylates and barbiturates, especially phenobarbitone and barbitone, which are normally removed only by the kidneys.

CASE I.—A woman, aged 50 years, was deeply unconscious 24 hours after the ingestion of a number of barbitone capsules. She had a previous history of recurrent attacks of pyelonephritis, and had been treated with penicillin and sulphonamides for an attack one week previously. When admitted to the Clinical Research Department, Sydney Hospital, she was deeply comatose and cyanosed, with very shallow slow respirations and mucopurulent secretions in the bronchial tree. Her muscles were generally flaccid, and all reflexes were absent. Her blood pressure was 130/80 millimetres of mercury. A sample of urine was green in colour and showed moderate proteinuria. Although she had had nothing to drink, the specific gravity was only 1·016, and barbiturates were present on analysis. Tracheal intubation and suction relieved her cyanosis and revealed signs of consolidation and pleural effusion at the right lung base. Because of the evidence of renal disease and of pulmonary complications, dialysis was considered advisable to remove the excess of barbitone. She was dialysed immediately for nine hours. After the first three hours her state of consciousness improved steadily. After five hours her respiration was of normal depth and had increased in rate, and she was no longer cyanosed. Her reflexes and muscle tone returned and by the end of the dialysis she was conscious and answering questions. She was quite cooperative and easy to nurse, but felt a little confused for three days. Her chest infection cleared completely in three weeks, after a course of penicillin and physiotherapy. Renal function was found to be impaired; there was persistent proteinuria, microscopic hæmaturia, maximum urine concentration to 1·012, a blood urea level of 47 milligrammes per 100 millilitres, and a urea clearance of 60% of the maximal average. She was discharged home from hospital clinically well and was referred for psychiatric guidance.

Preparation for Surgery.

Major surgery or urological investigative procedures may be indicated for the diagnosis or treatment of patients who are severely uræmic, but the procedures may be hazardous in their state of severe illness. In such cases, dialysis offers a safe means of alleviation of the biochemical disorder for several days or even weeks, thus enabling surgical treatment to be employed. Similarly, patients with chronic renal failure may be tided over an acute exacerbation due to pyelonephritis, gastro-enteritis or dehydration and salt loss.

CASE XI.—A man, aged 62 years, had had a suprapubic prostatectomy, followed by routine post-operative injections of penicillin and streptomycin. He passed very little urine after the operation, so that five days later his bladder was reopened and some stitches were removed. He remained severely oliguric and was transferred after seven days to the Clinical Research Department, Sydney Hospital. He had received a total dose of six grammes of streptomycin. He appeared drowsy and confused, with acidotic breathing, muscular twitching and hyperreflexia. The jugular venous pressure was raised and pitting œdema was present over the sacrum. His blood pressure was 170/100 millimetres of mercury. The heart was not enlarged and the eye grounds were normal. On cystoscopic examination the trigone of the bladder was swollen and red, and the ureteric orifices could not be seen. There was tenderness in both loins, especially on the right side. It was thought that the ureters were obstructed, perhaps as a result of previous calculus or other renal disease or as a result of the prostatectomy, and that further surgery would be necessary. In view of this and the toxic levels of streptomycin present, he was dialysed immediately, and dialysis was continued for nine hours. The next day he had no symptoms of uræmia, all signs of congestive failure had gone, and his weight had fallen 2·1 kilograms. Four days after dialysis, with increased tenderness over the right kidney and persisting oliguria, a right pyelostomy was performed. The pelvis was found to be dilated and contained 120 millilitres of urine. In the next 24 hours he passed 2250 millilitres of urine from the pyelostomy tube. Excretion then commenced from the left kidney as well. Two days after the relief of the obstruction his glomerular filtration rate was 50% of normal. He became somewhat dehydrated by his diuresis and was suffering from pneumonia. After six days of diuresis the serum urea level was 85 milligrammes per 100 millilitres, and he developed cardiac arrhythmia. He was very ill and emaciated, but improved after rehydration and the administration of digitalis and procaine amide. After this he slowly recovered. The nephrostomy and then the cystostomy tubes were removed and the wounds gradually healed spontaneously. Five weeks after his original operation both ureteric orifices could be seen on cystoscopic examination. The left ureter was easily catheterized, but the orifice of the right ureter was drawn upward and laterally, and could not be catheterized. However, after nine weeks both ureters could be catheterized, an intravenous pyelogram showed normal dye excretion from both kidneys, and the glomerular filtration rate was normal. He was still six kilograms (one stone) underweight. He had no signs of vestibular damage and his responses to caloric stimulation were normal.

This case illustrates the value of dialysis in the preparation of a severely uræmic patient for essential surgical treatment.

Conclusion.

The principle involved in the artificial kidney is sound in theory, and the results described above indicate that it is effective in practice. But what are the dangers in this form of treatment? Obvious hazards include the risks of hæmorrhage, either from some part of the body because of heparinization, or from rupture of the cellulose membrane in the machine; thrombosis and embolism; infection; untoward reactions to foreign blood; hæmodynamic disturbances associated with the imposition of an extracorporeal circulation; and biochemical mishaps through faulty concoction of the dialysing fluid. These are very real, and the operators must be continually on guard against them. With the aid of protamine sulphate, care in the sterilization of the blood-containing tubes, antibiotics, rapid and accurate biochemical checks and, above all, an experienced team of operators, the dangers are considerably reduced, and are probably no greater than the risks to be run in the worsening uræmia of prolonged anuria or in the other conditions in which dialysis is indicated The only troubles encountered in our series to date have been brief rigors, possibly due to pyrogens, in two of our early cases, and a small leak in the dialysing tubing in one other. As so often is the case with blood transfusion, so with dialysis; there are possible disadvantages as well as advantages, and it is a matter for careful assessment whether the treatment is indicated or not.

What are the contraindications? These are few, and relate to the dangers incurred by heparinization and by the extra load imposed on the patient's circulatory system. Thus, an active peptic ulcer or a history of hæmatemesis or other bleeding may contraindicate dialysis. So, too, may recent myocardial infarction or other cardiac disability.

The main indications for dialysis have been discussed in the body of this report—severe uræmia and acidosis, dangerous hyperkalæmia (especially if not easily or quickly controlled by exchange resins), overhydration, accumulated poisons which are dialysable, and the alleviation of uræmia in the preparation for some surgical procedure. Treatment is of most benefit in acute reversible conditions or in chronic conditions in which there is a superimposed process, which is conceivably self-limiting. Dialysis helps to reduce distress and to preserve life, even if it can play no part in curing the primary cause of the illness.

Naturally, dialysis finds its greatest use in acute renal failure, but it cannot be over-emphasized that it is but one item in the comprehensive care of these patients (Edwards, 1957; Edwards and Whyte, 1958). Treatment of the initiating cause, sustenance with the proper amount of water (usually as little as 400 ml. per day) and of food free from protein, sodium and potassium, the prevention of infection, the alleviation of symptoms and the careful correction of abnormalities in water balance and electrolyte levels are all important elements of treatment in the oliguric phase. Many anuric subjects can be successfully carried through their illness with proper conservative treatment without the use of an artificial kidney. Indeed, the majority of those patients requiring dialysis do so because of improper treatment, having been given excessive quantities of water, food containing salt and potassium, or streptomycin. However, besides these there are some patients with acute oliguric renal failure, who have received the best of conservative treatment and yet require dialysis. These include patients with prolonged anuria, those who develop the additional burden of complications or are in urgent need of surgical treatment, and those in whom a rising level of potassium is irrepressible, as sometimes occurs in the crush syndrome. In the final analysis, it stands to reason that the ideal way of dealing with accumulated toxic substances, if the accumulation cannot be prevented, is to remove the offending substances. If the artificial kidney will do this without undue danger, then it is a useful addition to our therapeutic armamentarium.

Summary.

The Alwall-type artificial kidney as installed in Sydney Hospital is described. Indications for its use occur most commonly in acute oliguric renal failure, and include severe uræmia, dangerous hyperkalæmia, overhydration, retention of poisons such as streptomycin, and the preparation of a uræmic patient for surgery. Its effectiveness is illustrated by reports of cases.

Acknowledgements.

We are grateful to the nursing staff, particularly Sister M. Gustafson, for invaluable help, to Mr. D. G. Failes and Dr. F. D. Collins for surgical assistance, to Miss Iris Yee and Miss M. Bell for technical assistance, to the Red Cross Blood Transfusion Service for its ready cooperation, and to various members of the staff of Sydney Hospital for their interest and help in many directions.

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A SURVEY OF WOUND INFECTION AT THE ROYAL MELBOURNE HOSPITAL.

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A SURVEY of wound infections was recently carried out at the Royal Melbourne Hospital, to determine the incidence of infection in wounds uninfected at the time of operation. The need for information on this subject has been stressed from time to time over the past few years in the medical literature. It is, therefore, thought that a report of the findings in this hospital might be of interest. No special prevalence of wound infections at the time prompted the investigation.

Material and Methods.

The series comprised 448 patients throughout the surgical wards of the hospital. Only wounds considered "clean" at operation were included in the survey. These were divided into two categories, first, those regarded as clean and without features predisposing to infection; secondly, those clean at operation but considered potentially infected. The first group included such procedures as herniotomy, thyroidectomy, and most orthopædic, thoracic and neurosurgical operations. The second group comprised mainly cases in which the gastro-intestinal tract was opened at operation. No colostomy wounds or urological procedures were included in the series.

The wounds were all inspected by one of us (M.R.), except for some of the neurosurgical cases, in which this arrangement proved impracticable. In these cases the information required was obtained from the doctor looking after the patient. The degree of infection was graded according to the following criteria: (*a*) no infection; (*b*) a little purulent discharge (grade I infection); (*c*) moderate amount to much pus, generally with gaping wound edges (grade II infection). Thus infection was assessed on clinical, not bacteriological grounds. However, when swabs were sent to the laboratory, the results of culture were included in the report.

TABLE I.

Wounds.	Number Infected.	Grade of Infection.
A: Clean wounds—357	21 (5·9%)	I. 9 II. 12
B: Potentially infected wounds (all general surgical)—91.	15 (16·5%)	I. 8 II. 7
A and B: All wounds clean at operation—448.	36 (8·0%)	I. 17 II. 19

Results.

The incidence of wound infection is set down in Table I. There were 357 wounds clean at operation and considered of such nature as not liable to contamination; of these 21 (5·9%) became infected, the infection in nine being of grade I severity and in 12 of grade II. There were 91 wounds clean at operation, but regarded as potentially infected; of these, 15 (16·5%) became infected; eight were classified as grade I and seven as grade II infections. The total number of patients whose wounds were considered clean at operation was 448. Thirty-six wounds (8%) subsequently became infected, 17 being grade I and 19 grade II infections.

TABLE II.

Data on Clean Wounds that Became Infected.

Operation.	Grade of Infection.	Infecting Organism(s) and Sensitivity.
Pneumonectomy ..	II	*Staph. aureus* P−S−C+T−E+[1]
Aortic valvotomy ..	II	*Staph. aureus* P−S+C+T+E+
Mitral valvotomy ..	I	*Staph. aureus* P±S±C+T+E+
Laparotomy	I	*Staph. aureus* P−S−C+T−E+
Laparotomy	I	*Staph. aureus* P+S−C+T−E+
Cholecystectomy ..	I	*Staph. aureus* P+S+C+T+E+
Hiatus hernia repair ..	II	No culture.
Hysterectomy	II	*Staph. aureus* P−S−C+T−E+
Insertion of T. King nail and plate.	I	No culture.
Insertion of T. King nail and plate.	II	*Staph. aureus* P±S+C+T+E+
Revision of cup arthroplasty.	II	*Staph. aureus* P±S−C+T−E+
Cup arthroplasty ..	II	*Staph. aureus* P±S+C+T+E+
Girdlestone operation ..	I	*Staph. aureus* P−S−C+T−E+
Kirschner wire insertion	I	*Staph. aureus* P−S+C+T+E+
Craniotomy	II	*Bacterium coli.*
Ligation of cerebral aneurysm.	II	*Bacterium coli* S−C+T+O−
Ligation of cerebral aneurysm.	II	*Bacterium coli* S+C+T+O+
Posterior fossa decompression.	I	No culture.
Dissection of inguinal glands.	II	*Staph. aureus* P−S−C+T−E+
Radical mastectomy ..	II	*Streptococcus faecalis* P−S−C−T−E− *Bact. coli* S−C+T+O+
Radical mastectomy ..	I	No culture.

[1] P, penicillin; S, streptomycin; C, chloramphenicol; T, tetracycline; O, oxytetracycline; E, erythromycin; "+", sensitive; "±", partially sensitive; "−", resistant.

Tables II and III give data on those patients who developed wound infections. In each case the operation, grade of infection and, when known, the infecting organism and its sensitivity pattern are given. Among the clean wounds that became infected, there were three thoracic, four abdominal, one gynæcological, six orthopædic and four neurological operations, one dissection of inguinal glands and two radical mastectomies. In the last two cases the condition of the tissues was highly favourable to bacterial colonization; they were not, however, counted in the category "potentially infected".

TABLE III.

Data on Potentially Infected Wounds that Became Infected.

Operation.	Grade of Infection.	Infecting Organism(s) and Sensitivity.
Relief of small bowel obstruction.	I	*Staph. aureus* P±S−C+T+E+[1]
Partial gastrectomy ..	II	No culture.
Partial gastrectomy ..	I	No culture.
Partial gastrectomy ..	I	No culture.
Anterior resection of rectum.	I	No culture.
Partial gastrectomy ..	I	*Staph. aureus* P+S+C+T+E+
Colectomy	I	*Bact. coli* S−C+T±O±
Repair of hiatus hernia and subtotal gastrectomy.	II	*Staph. aureus* P−S−C+T+E+ *Pseudomonas pyocyanea* S−C−T−O−
Partial gastrectomy ..	II	*Bact. coli* S−C+T−O−
Subtotal gastrectomy ..	II	*Bact. coli* S−C−T−O−
Transthoracic gastrectomy	I	*Staph. aureus* P−S−C+T+E+
Partial gastrectomy ..	II	No culture.
Excision of Meckel's diverticulum.	I	*Bact. coli* S+C+T+O+
Partial gastrectomy ..	II	*Staph. aureus* P−S−C+T+E+
Enteroanastomosis ..	II	*Bact. coli* S−C−T−O−

[1] See footnote to Table II.

All 15 potentially infected wounds in which infection developed were in patients who had had an operation on the gastro-intestinal tract.

The results of the wound cultures available are summarized in Table IV. In the majority of cases the infecting organism was *Staphylococcus aureus*, this species being cultured from 13 out of the 18 clean wounds and from five of the 10 potentially infected wounds from which swabs were examined.

TABLE IV.

Infecting Organisms.

Source of Organisms.	*Staph. aureus.*	*Bact. coli.*	Other Species.
Clean wounds (18/21 swabbed) ..	13	4	1
Potentially infected wounds (10/15 swabbed)	5	5	1

Discussion.

Results of surveys to determine the precise incidence of wound infection have frequently yielded a figure higher than anticipated. Meleney, at the Presbyterian Hospital in New York, records a senior surgeon as giving as his estimate of wound infection in his unit an incidence of 2%, when subsequent investigation showed it to be 14%.

After the present survey had been completed, an attempt was made to compare the findings with those of other published series. This proved difficult in some instances, as the criteria of infection were not always clearly indicated. However, a number of surveys considered comparable with ours are listed in Table V. The survey reported from the Edinburgh Royal Infirmary was published about the time of completion of our own, and is probably the one that is most comparable with ours. It covered four surgical charges of the hospital—one orthopædic, one neurosurgical and two general surgical. The infection rate was separately assessed for those wounds regarded as clean, and for those that were clean but

TABLE V.
Reported Surveys of Wound Infection Incidence.

Investigators.	Hospital.	Year(s).	Number of Wounds.	Percentage of Infections.		
				Major.	Minor.	Total.
Meleney (1940)	Presbyterian Hospital, New York.	1925	558	4·0	10·0	14·0
		1939	1725	0·6	2·0	2·6
Ives and Hirshfield (1938) ..	New Haven Hospital.	July, 1934, to April, 1937	1361	—	—	5·29
Howe (1954)	Massachusetts Memorial Hospitals, Boston.	1940	401	1·24	0·75	1·99
		1953	429	4·66	2·56	7·22
Clarke (1957)	Bristol Royal Infirmary.	1953	382	6·5	7·1	13·6
Jeffrey and Sklaroff (1958) ..	Edinburgh Royal Infirmary.	1956	673	7·7	2·1	9·8
Present series	Royal Melbourne Hospital.	1957–1958	448	3·8	4·2	8·0

potentially infected. The infections were graded as trivial (redness at the wound edge or at stitch holes), moderate or severe. The last two correspond to grades I and II of the present series. In our cases, redness of the wound alone was not counted as infection. The over-all incidence of moderate and severe infections in the Edinburgh series was 9·8% (comparable to our incidence of 8·0%). The incidence among the clean, not potentially infected wounds was 4·5% (ours 5·9%). The range in the Edinburgh series over the four surgical charges was as follows: orthopædic 0·8%, neurosurgical 5·2%, general surgical I 11·1%, general surgical II 4·0%. The infection rate among the orthopædic patients is indeed admirably low, and suggests that conditions in this unit are in some way different from those on the other units. The authors do not state that such is the case, though they express the opinion that the hospital average would probably have been higher if all six general surgical units rather than just two had been included in the study. Comparable subdivision of our cases cannot be made, except for the neurological cases, which form a separate unit. The incidence of infection in this group (110 patients) was 3·6%. In the group of potentially infected wounds in the Edinburgh series, the average incidence was 19·2% (orthopædic 20%, neurosurgical 7·1%, general surgical I 18·4%, general surgical II 23%). The incidence among our patients in this category was 16·5%.

Although the survey was instituted as a clinical assessment of the wound infection position in the hospital, some comment may be made on the laboratory findings. As was anticipated, the infecting organism in most cases was *Staph. aureus*. In five of the 18 cases the antibiotic sensitivity pattern was that most frequently encountered in the hospital—namely, resistant to penicillin, streptomycin and tetracycline, and sensitive to chloramphenicol and erythromycin. Such cases are clearly cases of hospital cross-infection, as also presumably are the infections in the neurological wounds. Some at least of the infections following gastro-intestinal operations are likely to be due to auto-infections. No death was directly attributable to wound infection. Prolongation of hospital stay due to wound infection could not be assessed, because of the presence of other complicating factors in these cases.

In general, the results of the survey compare not unfavourably with the findings of other investigations. Most of these, it can be seen, depart widely from the figure of 1% to 2% quoted in the past as the accepted incidence of infection in clean wounds. It seems likely that in practice such a standard is rarely achieved. However, our present incidence is undesirably high and warrants more detailed and extensive investigation into the contributory factors.

Summary.

The incidence of infection in clean wounds was investigated at the Royal Melbourne Hospital.

Infection was assessed on clinical, not bacteriological grounds. Any purulent discharge counted as infection. Redness alone was disregarded.

There were 448 clean wounds altogether; 357 were considered clean and not liable to contamination; 91 were clean at operation but regarded as potentially infected (e.g., the operation involved opening the gastro-intestinal tract). In the first group 5·9% became infected and in the second group 16·5%, giving an overall incidence of infection of 8% in all wounds clean at operation.

The results of cultures from swabs when these were taken showed that the majority of infections were due to *Staph. aureus*.

These findings are compared with some other published series of similar surveys.

Acknowledgements.

We are grateful to the members of the honorary medical staff of the Royal Melbourne Hospital for their cooperation in this investigation, and for permission to publish the findings. It was at the suggestion of some of them that the project was initially undertaken. We are also grateful to the members of the nursing staff for their willing cooperation throughout. We should also like to thank Professor R. R. H. Lovell for advice in regard to the plan of conduct of the survey.

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WOUND INFECTIONS.[1]

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FOUR years ago at a city hospital, a woman underwent triple fusion of both feet. Shortly afterwards gas gangrene developed in one foot. A below-knee amputation was performed. She now walks well with a prosthesis, but suffers recurrent stump pain.

About five years ago at another major city hospital, a Judet type of arthroplasty was performed on the hip of a man suffering from ankylosing spondylitis. It became infected with *Staphylococcus aureus*. The prosthesis was removed; but the patient suffered from a persistent sinus with recurrent acute attacks of infection which necessitated frequent admission to hospital until his death a few weeks ago.

It is fortunate that only the occasional wound infection produces such a dramatic story. Life is rarely threatened; but the importance of wound infection cannot be minimized when its results in terms of morbidity and impaired

[1] Read at a meeting of the New South Wales Branch of the British Medical Association on November 27, 1958.

function are assessed. I intend to confine my remarks to infections arising in "clean" wounds after elective surgery, because in a sense they are iatrogenic and should therefore be preventible.

That infection occurs in every surgical unit no one will deny, but how frequently it occurs can be determined only by recording it. Guesses are always low. That it occurs to any extent in an orthopædic surgical unit, when chronic infection and fibrosis mean losses in terms of function, is deplorable.

There are many figures available for the incidence of wound infection in surgical units. Some local ones are of interest. At the Royal North Shore Hospital of Sydney over a six-month period in 1958, 19·8% of wounds became infected in 440 cases. This was an entirely unselected series. Of these infections, 17% were classed as minor and 2% were classed as major. At the Royal Prince Alfred Hospital during 1958, 8% of wounds became infected. This, however, was a selected series, from which were excluded those cases in which infection or potential infection was present prior to operation. At the Robert Jones and Agnes Hunt Orthopædic Hospital, Oswestry, over a twelve-month period in 1955, a wound infection rate of 6% was found. This again was a selected series, and being such, is indicative of the true rate of possibly preventible surgical infections.

During the period from January to June, 1958, a wound infection register was kept in the orthopædic unit of the Royal North Shore Hospital. A record was kept of all wounds that became infected. All infected wounds were swabbed and the organisms grown were tested for their antibiotic sensitivities. The decision as to whether a wound was classified as infected was not made by the surgeon who operated on the patient, and all cases were classified by one person. The criteria on which wounds were classified as infected were as follows: (i) Serious infections—e.g., abscess formation, marked cellulitis, purulent discharge. These were the obvious wound infections. (ii) Minor infections—e.g., failure to heal by first intention, redness about the wound edges with or without purulent or seropurulent discharge; absence of constitutional evidence of infection was disregarded. These wound infections were in reality minor, in that wound healing was not appreciably delayed and there was no apparent functional impairment. Minor infections should be included in any series so that an index of the total infection rate can be gained. A false sense of security may otherwise be engendered.

The second group of wound infections is difficult to define accurately, as all those who have attempted to do so will agree. In fact, such difficulty may well account for the discrepancy in figures from different centres. I adopted the strictest criteria, similar to those adopted in the survey at the Robert Jones and Agnes Hunt Orthopædic Hospital, Oswestry, so the two series can be compared. In the period under review, 118 "clean" patients underwent elective surgical procedures. All patients suffering from infection pre-operatively were excluded from the series as well as those potentially infected—e.g., those having bone grafts to old compound fractures or those with compound fractures themselves. Of these 118 patients, operated upon by five different surgeons, eight became infected. One of these was classed as suffering from a serious infection, and the other seven were recorded as having minor infection. This gives an infection rate of 6·8%. The total number is too small to allow further breakdown. This figure is much in accord with that from Oswestry.

After an orthopædic procedure, the vast majority of patients have either a plaster cast or a pressure bandage applied. Neither of these is removed until well after wound healing. This may account for the difference in wound infection rates when compared with abdominal surgical cases in two ways: (i) Because of the rest and splintage, the body is better able to deal with a contaminated wound. (ii) If ward infection is important, the occlusive dressing prevents contamination in the ward by either team or patient.

However, generally orthopædic surgeons are far more conscious of the results of wound infections, and the lower rates are probably indicative of their better aseptic techniques.

From five of the eight infected wounds in this series was grown *Staphylococcus aureus*, coagulase-positive. Swabs from two of the wounds were sterile. Phage typing of the staphylococcus was not performed.

Apparently, wound infection with *Staph. aureus* is usually fairly benign, but this is dependent on the local conditions in the wound. These local factors are influenced by the surgeon, and are reflected in the repair rate in two ways. First, contamination of wounds containing foreign bodies such as plates, screws, bone grafts, etc., is likely to produce a serious infection, so that even greater care should be taken when such materials are used. Secondly, many minor wound infections are produced by such things as necrosis from tight skin stitches, non-viable skin flaps, hæmatomata providing an excellent culture medium for a ubiquitous organism. In these wounds the infection is of secondary importance and can be reduced by strict attention to good surgical practice.

Although our infection rate of 6·8% is acceptable when compared with other figures, no one can be satisfied that one in fifteen of all clean operative wounds becomes infected, particularly in view of the increasing resistance of the hospital staphylococcus to antibiotics.

Most observers agree that the majority of wounds, if not all, are infected during operation. The factors surrounding this event must therefore be examined to determine the source of the organisms: First, the paraphernalia used in the operation; secondly, the surgical team; thirdly, the air in the operating theatres; fourthly, the patient himself. I do not propose to say much about the first source of infection, except to comment that high-pressure sterilization is a modern "must", and that moisture about the operative field invites trouble. Linen drapes fail as barriers to organisms when damp. Sponges washed out in a bowl of water which is easily contaminated are suspect. A minor outbreak of infection in the orthopædic unit at Royal North Shore Hospital was apparently controlled by a change from wet to dry sponges and swabs. This was an impression; I can give no figures, as it occurred before a record of wound infections was kept.

The surgical team figures probably very largely in the introduction of bacteria to open wounds. In February, 1958, nasal swabs were taken from all members of the obstetric staff at the Royal North Shore Hospital. Of 73 swabs, 33 grew coagulase-positive *Staph. aureus*. This is a carrier rate of pathogenic *Staph. aureus* by the staff of 45% and agrees with the best figures produced by Blowers.

Recently the dorsum of the hands of a surgeon were swabbed. On October 8, 1958, before scrubbing, five colonies of *Staph. aureus* were cultured. After eight minutes' scrubbing, 26 colonies of hæmolytic *Staph. aureus* were grown. After 45 minutes of wearing gloves, one colony of hæmolytic *Staph. aureus* was grown. It would appear that some technical fault was to blame for the distribution of organisms, so that on November 3, the swabbings were repeated. Before scrubbing, two colonies of hæmolytic *Staph. aureus* and *albus* were grown. After scrubbing, no colonies were grown. After 90 minutes of wearing gloves, two colonies of hæmolytic *Staph. aureus* and *albus* were grown. At the time of the first swabbings the surgeon was suffering from an upper respiratory tract infection, which may have accounted for the high concentration of organisms encountered.

How many of us are aware what our skin flora is, or how it may change over the years? If we bear in mind the rate of glove puncture (about 15%), this must suggest that a continuation of the no-touch technique is of value.

Much has been said about air-borne infection. No doubt it plays a large part in cross-infection in hospital—just how large a part is difficult to define. At St. Bartholomew's Hospital, a dramatic reduction in the number of wound infections occurred when the exhaust type of ventilation,

which sucked air into the operating theatres from the surrounding corridors and wards, was replaced by a plenum or positive-pressure system of ventilation. It has been shown elsewhere, however, that provided a plenum ventilating system is used, the reduction of colony counts of theatre air, which usually are between 10 and 20 per cubic foot, has no effect on the wound sepsis rate.

Apparently air-borne infection plays little part in the genesis of wound infection, provided (i) a positive-pressure system of ventilation is used and (ii) air for this system is drawn from the atmosphere some distance from the ground and wards, preferably from the roof.

Of course, the patient himself may be the source of the infection. If that is so, organisms may be derived from (*a*) bacteriæmia, (*b*) the surrounding skin, (*c*) clothing or ward blankets.

One would expect blood-borne infection, if it occurred, to have approximately the same frequency as the infection rate of closed fractures. Certainly the closed fracture produces as much hæmatoma and soft-tissue damage as does the usual type of operation, and could be regarded as an ideal pabulum for organisms deposited from the blood-stream. Just what the infection rate of closed fractures is I do not know and a have not been able to determine, but it must be infinitesimal. Of one thing I am sure, that it must not approach the infection rate of surgical wounds. Further, surgery is not performed in the presence of demonstrable infection elsewhere in the body, so that the rate must be further substantially reduced. I believe that this type of infection, if it does occur, can be discounted as contributing significantly to the general infection rate. Blankets from the wards should be barred from the operating theatres, and proper attire for the patient insisted upon.

I was prompted by the comment of an anæsthetist, about to anæsthetize a patient whose limb had been wrapped in sterile towels after a ward preparation of the skin, to inquire into the efficacy of such a procedure. The anæsthetist made the comment that it appeared to be a lot of trouble and discomfort for the patient for so little value. During the latter part of 1958, investigation of the efficacy of skin sterilization procedures has been carried out in the orthopædic unit of the Royal North Shore Hospital. The preparation of the patient's skin for operation in this unit is carried out, first, by shaving the part as necessary and instructing the patient to bathe. This is carried out 48 hours prior to operation. After this a skin preparation is carried out by a nurse who is gowned and masked and has "scrubbed up". A sterile drawsheet is laid underneath the patient's limb, which is then swabbed with the use of a no-touch technique, with: (i) ether soap, (ii) sterile water, (iii) 70% alcohol, (iv) skin ether.

The limb is then wrapped in two layers of sterile towels, and the drawsheet is used to enclose the towelling. The drawsheet is pinned with sterile pins. This procedure is carried out the next day and then on the morning before the operation. Immediately prior to operation, the skin is painted with a solution of 2% iodine in 70% alcohol. This is allowed to dry. The iodine is then washed off with 70% alcohol.

A series of skin swabbings were taken and skin biopsies done. The swabbings have shown a marked reduction in the concentration of skin organisms after the preparation. Furthermore, in a very high proportion of cases the skin biopsy specimen has been sterile. At present the number of patients investigated in this manner is too small to allow definite conclusions to be drawn, but the series is at present being expanded.

It has often been taught that skin sterilization is not possible, in that organisms survive deeply in the skin crevices—hair follicles and sweat glands. If the results in these few cases are confirmed, it is apparent that skin can be sterilized if an adequate technique is used.

In view of the foregoing findings, it must be assumed that organisms from the patient's own body can play only a minimal part in the wound sepsis rate, and efforts to reduce the rate have to be made in other and more fruitful directions.

Summary.

It has become apparent to me in the course of the last six months that, although the origins of the hard core of some 6% to 10% of surgical wound infections have been extensively documented, at the moment it is quite impossible to impugn dogmatically one particular source. It is possible that infection from the air is of small significance. It is unlikely that the patient himself is the origin of the infection. In a properly run theatre organization it should not come from the theatre equipment, etc. Possibly the answer lies in organism carriage by the surgical team. It would be impracticable to exclude all carriers of *Staph. aureus* from the theatre team, in view of the high rate of carriage of this organism; but there is a strong case for the continuance of a no-touch technique. Adequate masking is essential, together with changing of masks at the end of each operation.

It would be wrong to develop a fad about the source of wound infection, as the problem is complex and each factor must be dealt with in turn.

Over-all, our responsibility lies in insisting on the highest known standards of aseptic technique.

Acknowledgements.

I wish to thank the General Medical Superintendent and the honorary orthopædic surgeons of the Royal North Shore Hospital of Sydney for permission to publish these figures. I also wish to acknowledge my debt to the Director and members of the staff of the Kolling Institute, without whose assistance there would have been no evidence.

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LONG-ACTING PROGESTERONE PREPARATIONS AND ORALLY ADMINISTERED "PRIMOLUT N" IN THE TREATMENT OF HABITUAL ABORTION.[1]

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Corpus luteum therapy has proved valuable in the treatment of patients who have had recurrent abortions as the result of progesterone deficiency. Progesterone given intramuscularly rapidly raises the pregnanediol excretion and therefore presumably the blood progesterone level; but daily injections are necessary to maintain it at a constantly rising level. If marked falls occur, there is always the chance of threatened or actual abortion.

Ethisterone (anhydro-hydroxy-progesterone) has proved effective in producing results similar to those of progesterone. Buccal absorption is much more efficient than oral ingestion. By the former method four-fifths of the dose is absorbed into the general circulation, and is therefore available in the uterine area before it passes to the liver, where it is converted to pregnanediol glycuronidate. This compound is then excreted in the urine. By the latter method, only one-fifth of the ingested ethisterone behaves in this way. Ingestion of large doses of ethisterone—e.g., 200 milligrammes per day—by patients with

[1] This work was made possible by a grant from the National Health and Medical Research Council to one of us (V.I.K.).

gross progesterone deficiency becomes irksome. Claims that other corpus luteum preparations—e.g., progesterone implants, "Lutocyclin" and "Proluton-Depot"—would maintain the blood progesterone level for several weeks promised an improvement in the treatment of these patients, and tests were commenced in 1954. "Primolut N", another progesterone derivative for oral ingestion with biological activity claimed to be ten times as great as that of ethisterone, has also been investigated in a small series of patients.

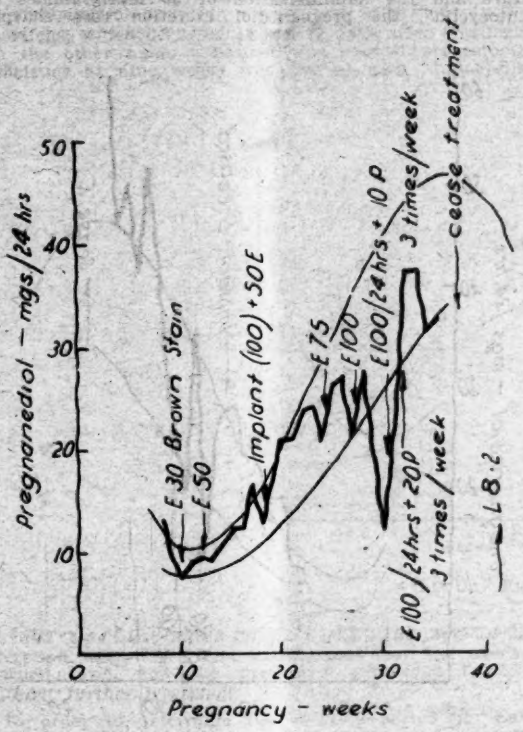

FIGURE I.

Previous abortions: four between eight and twelve weeks. Premature rupture of membranes in last pregnancy at 38 weeks, with ethisterone treatment, but only five milligrammes per day.

The Value of Implants of Progesterone Pellets.

Bishop and Richards (1952) obtained excellent results by implanting pellets of progesterone as early as possible in the pregnancy in patients who had a history of three or more consecutive abortions. Six 25-milligramme pellets were implanted beneath the deep fascia of the thigh. *It was thought that the progesterone level was* maintained for at least four weeks by this form of therapy. Twenty-three of their 32 patients produced living children during the current pregnancy.

We have tested the effect of implants on 12 progesterone-*deficient patients with histories of recurrent abortion. The* amount of pregnanediol excreted before and after insertion of 100 milligrammes of progesterone was determined. In two cases the pregnanediol excretion rose slightly during the next four weeks, but after that it could be maintained at the average normal level only by increasing the oral ethisterone dosage and finally by supplementing this with progesterone injections (see Figures I and II).[1] In the *other eight cases the weekly pregnanediol values fell* sharply after insertion of the implant (e.g., Figures III and IV).

Bishop and Richards (1952) treated all patients who had suffered recurrent abortions with progesterone implants. *Swyer and Daly (1953) treated alternate patients in a* similar series. There was no significant difference in these two groups of patients, none of whom was tested for progesterone deficiency. Bishop and Folley (1951) showed that the rate of absorption of 200 milligrammes of progesterone *implanted in female patients was about 40% in 40 days.* In Swyer and Daly's patients, only about three or four milligrammes would be absorbed per day. They concluded *that the amount was probably inadequate to tide* over the deficiency in the early weeks of pregnancy, when abortion frequently occurs. In our experience this amount would be inadequate for treatment of anything except the slightest progesterone deficiency.

"Lutocyclin."

"Lutocyclin" (anhydro-hydroxy-progesterone) is supplied in the form of micro-crystals in an aqueous suspension. A

[1] *The following abbreviations are used in the graphs* (Figures I to XXII): E, ethisterone; L, "Lutocyclin", DP, "Proluton-Depot"; PG, progesterone; Prim N, "Primolut N".

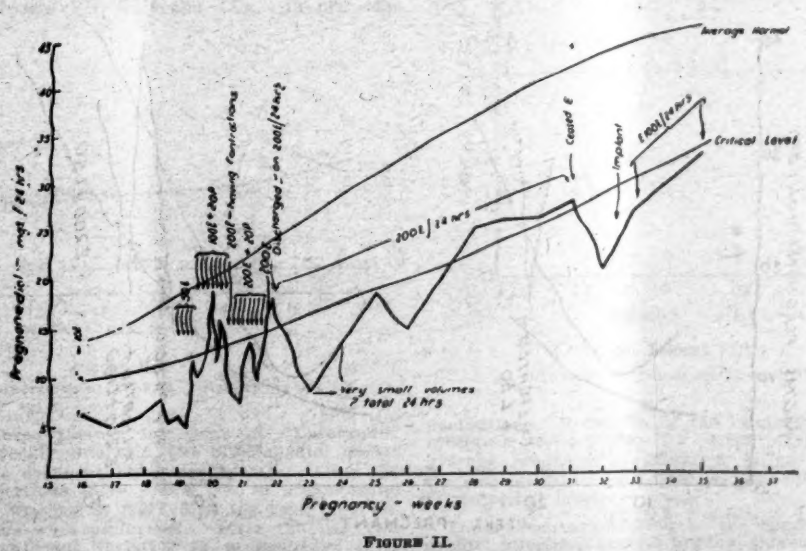

FIGURE II.

Previous abortions at 12, 13, 14 and 14 weeks.

dose of 50 milligrammes of "Lutocyclin" given intramuscularly was said to be effective for three weeks.

Since the excretion of pregnanediol has been found to be a useful guide in assessing the necessary dosage of progesterone by injection or buccal absorption, we have studied its value after the injection of "Lutocyclin" in 20 patients who suffered recurrent abortion.

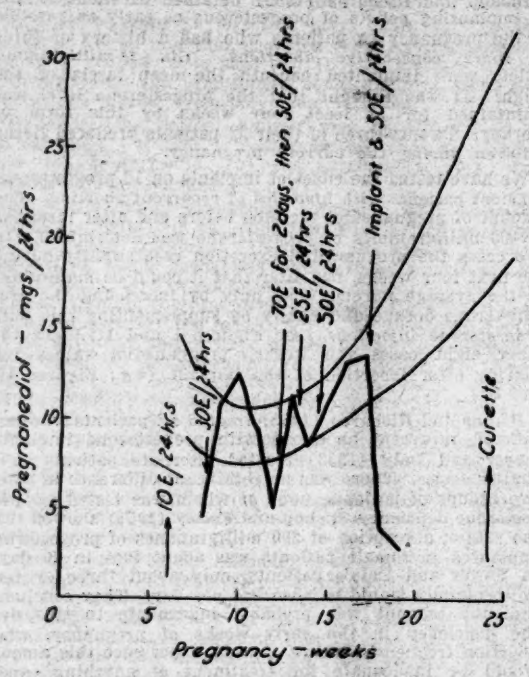

Figure III.
Previous abortions at 12 and 16 weeks.

The pregnanediol excretion per 24 hours, determined at weekly intervals following intramuscular injection of 50 milligrammes of "Lutocyclin", proved to be very variable in the cases studied. In some cases there was a definite rise. This is illustrated by two patients who had pregnanediol excretion falling to the critical level associated with dilatation of the cervix and bulging membranes. After suture and the administration of 50 milligrammes of "Lutocyclin", the pregnanediol excretion rose sharply

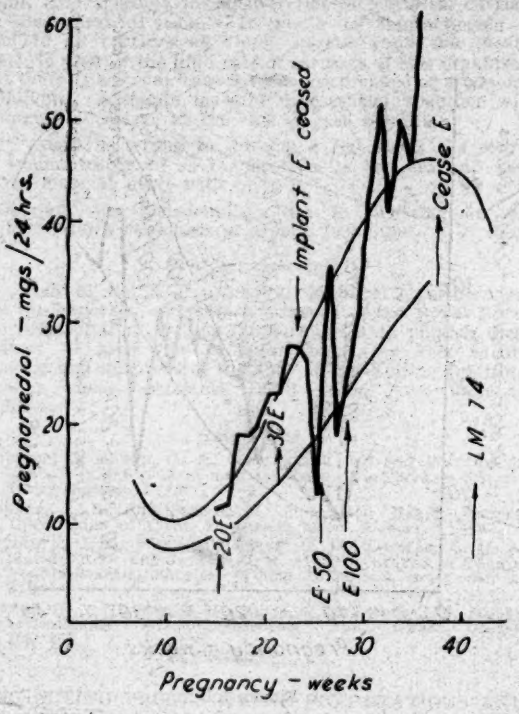

Figure IV.

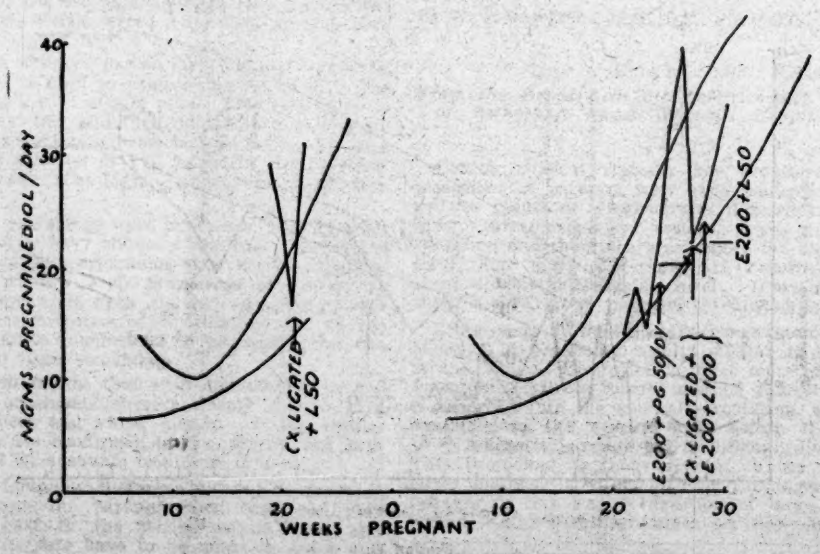

Figure V.

(Figure V). However, this was not a constant effect. Other patients showed no increase and some showed a fall in pregnanediol excretion after similar treatment. Some typical curves are shown in Figure VI.

Manufacturers at first stated that "Lutocyclin" remained effective for three weeks. In two patients treated prophylactically with 50 milligrammes of "Lutocyclin" because of a past history of recurrent abortion, very low levels of pregnanediol excretion were found to precede further abortions, which occurred 14 and 21 days after treatment. On the other hand, a patient who showed progesterone deficiency at nine weeks was treated with "Lutocyclin" at intervals of two weeks for six weeks. The pregnanediol excretion was raised and maintained near the average normal level, and the pregnancy proceeded to term without further treatment.

In order to determine the effective period of "Lutocyclin" activity, daily assays of pregnanediol excretion per 24 hours were made after the injection of 50 milligrammes of "Lutocyclin". After a single injection the pattern of pregnanediol excretion was similar in the three patients studied. The excretion rose for three to four days, and then fell to the pre-injection level by the seventh day (Figures VII, VIII and IX). In one case (Figure IX), three further injections of "Lutocyclin" were given at weekly intervals, but pregnanediol assays were made at the usual weekly intervals only. After the first of these injections there was a rise in pregnanediol excretion, which was not so marked as the peak observed when daily assays were performed. After the last two injections no significant variation in pregnanediol level was observed. It seems logical to infer that the rise in pregnanediol excretion after intramuscular injection of "Lutocyclin" is not prolonged, and may be missed unless urine is collected at the correct time.

The effect of frequent larger injections of "Lutocyclin" is illustrated in Figure X. This patient failed to respond to massive doses of ethisterone, progesterone and "Proluton-Depot". She also showed a poor response to a single injection of "Lutocyclin". For two weeks injections of 100 milligrammes were given daily. In daily assays the pregnanediol excretion was always well above the pre-treatment level, but there were marked fluctuations. Reduction of the "Lutocyclin" dosage to 50 milligrammes per day for seven days resulted in the average pregnanediol excretion falling midway between the average ethisterone level and the 100 milligrammes of "Lutocyclin" level.

These observations lead to the conclusion that "Lutocyclin" injections cause a gradual increase in pregnanediol

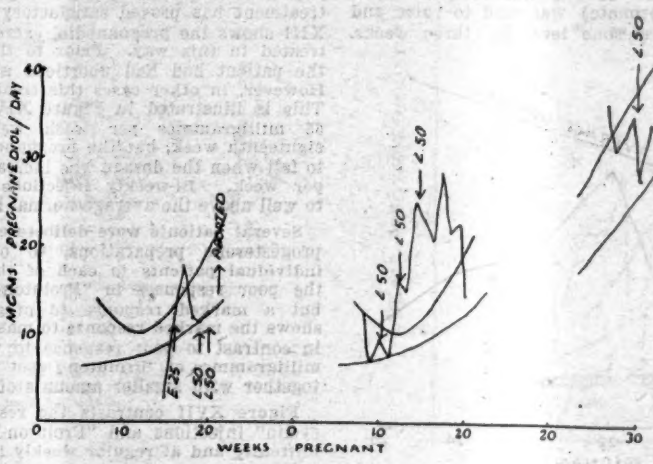

FIGURE VI.

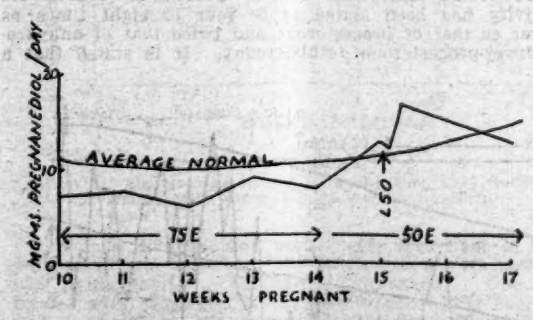

FIGURE VII.
Previous abortions at 27, 9, 6, 8 and 18 weeks.

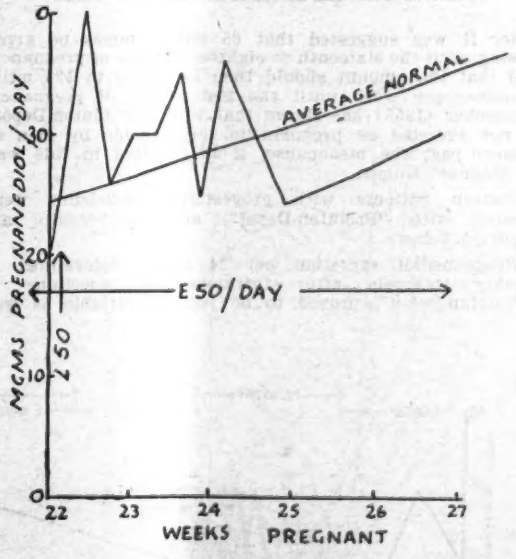

FIGURE VIII.
Previous abortions at 22 and 21 weeks.

excretion for three to five days, during which time the blood progesterone level is presumably raised. However, injections need to be given frequently, and probably in greater amounts than the manufacturers suggest, to prevent abortion in patients with marked progesterone deficiency. "Lutocyclin" therefore does not appear to be valuable as a long-acting product. In ethisterone-resistant patients, frequent "Lutocyclin" injections may prove effective in keeping the blood progesterone level sufficiently high to maintain the pregnancy.

"Proluton-Depot."

Intramuscular injection of "Proluton-Depot" (17-hydroxy-progesterone-17-capronate) was said to raise and maintain the blood progesterone level for three weeks.

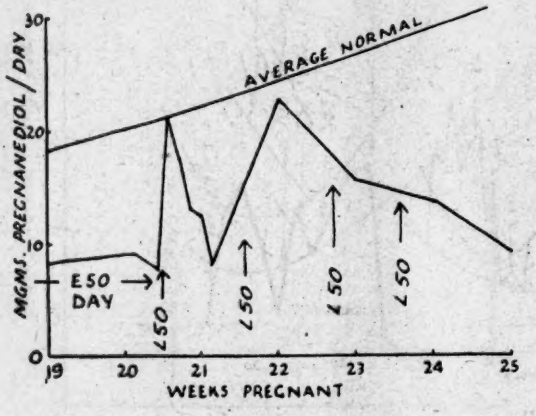

Figure IX.
Previous abortions at 16, 6, 20, 24 and 6 weeks.

Later it was suggested that 65 milligrammes be given weekly until the sixteenth to eighteenth week of pregnancy, and that the amount should then be raised to 125 milligrammes per week until the last month of pregnancy. Langecker (1955) has shown that whilst "Proluton-Depot" is not excreted as pregnanediol glycuronide by men or women past the menopause, it is excreted in this way by pregnant women.

Sixteen patients with progesterone deficiency were treated with "Proluton-Depot", and the results are reported below.

Pregnanediol excretion per 24 hours, determined at weekly intervals after intramuscular injections of "Proluton-Depot", proved to be just as variable as was found after similar treatment with "Lutocyclin". It rose in some cases and fell in others (Figure XI). Similarly, daily assays showed a gradual rise to about the fourth day, and a fall to the pre-injection level by the seventh day (Figure XII). In this case the pregnanediol excretion estimated at weekly intervals showed no rise after weekly injections. Like "Lutocyclin", "Proluton-Depot" causes a gradual rise in pregnanediol excretion, which is not prolonged for more than a few days.

It is now suggested by the manufacturers that injections of 65 milligrammes of "Proluton-Depot" should be given weekly until the eighteenth week, and then the dose should be increased to 125 milligrammes per week. This treatment has proved satisfactory in some cases. Figure XIII shows the pregnanediol excretion curve for a patient treated in this way. Prior to this successful pregnancy the patient had had abortions at 14, 18 and 12 weeks. However, in other cases this treatment was not adequate. This is illustrated in Figure XIV. It will be seen that 65 milligrammes per week were adequate until the eighteenth week, but the pregnanediol excretion continued to fall when the dosage was increased to 125 milligrammes per week. Bi-weekly injections caused a marked rise to well above the average normal level.

Several patients were deliberately treated with different progesterone preparations, to obtain the reactions of individual patients to each of them. Figure XV shows the poor responses to "Proluton-Depot" and ethisterone, but a marked response to progesterone. Figure XVI shows the marked response to massive doses of ethisterone, in contrast to poor response to weekly injections of 125 milligrammes of "Proluton-Depot" and of "Proluton-Depot" together with smaller amounts of ethisterone.

Figure XVII contrasts the response to random "Lutocyclin" injections and "Proluton-Depot" given both intermittently and at regular weekly intervals.

"Proluton-Depot" appears to be ineffective for more than a few days. In some cases weekly injections in the dosages suggested by the manufacturers have proved adequate, but the best results are obtained by determining the necessary amount and frequency of injections by weekly pregnanediol assays.

19 Nor-ethisterone, Anhydro-hydroxy-nor-progesterone or "Primolut N".

"Primolut N" or anhydro-hydroxy-nor-progesterone is a new progesterone derivative effective by oral administration. The compound possesses a high degree of biological activity. This has been demonstrated in animal experiments by Tullner and Hertz (1953) and by Herts, Tullner and Raffelt (1954), and clinically by Hertz, Waite and Thomas (1956) and also by Greenblatt (1956). Its activity has been stated to be four to eight times as great as that of progesterone and twice that of anhydro-hydroxy-progesterone (ethisterone). It is stated that a

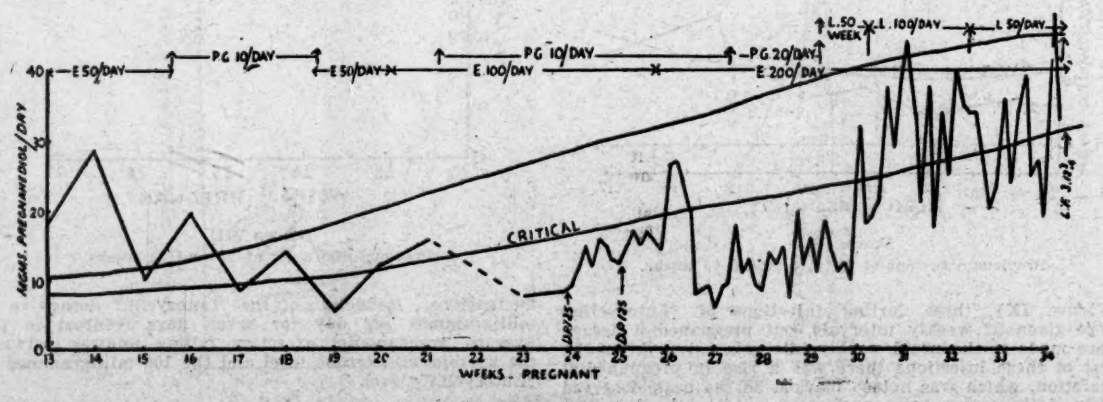

Figure X.
Previous abortions at 22 and 18 weeks.

secretory endometrium can be built up by ingestion of 10 to 15 milligrammes on each of 10 consecutive days. Morning temperature is elevated by "Primolut N" in the same ways as by progesterone therapy. Brochure (1957) states that "Primolut N" causes no significant rise in pregnanediol excretion.

It is suggested that one tablet (five milligrammes) of "Primolut N" should be taken twice a day by patients who have suffered repeated abortions, from the beginning of a pregnancy until approximately four weeks after the time when earlier pregnancies have terminated in abortion.

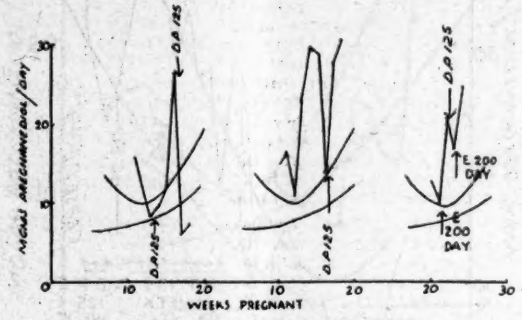

FIGURE XI.
Previous abortions: (a) 22 and 8 weeks; (b) 9, 9, 24, 19, 18 (full term) and 15 weeks; (c) 8, 20, 24, 20, 34, 22 and 15 weeks.

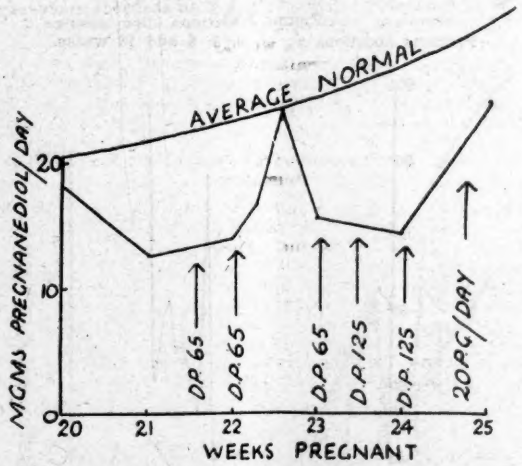

FIGURE XII.
Previous abortions at 13 and 14 weeks, then a 41 weeks' pregnancy with controlled ethisterone treatment.

"Primolut N" has been used in the treatment of nine patients in this hospital. Only four of these nine patients had living babies in the present pregnancy. One was treated with "Primolut N" for two weeks whilst abortion was threatening; the symptoms subsided. The second had empirical "Primolut N" treatment. The third was treated with "Primolut N" controlled by pregnanediol excretion estimations (Figure XVIII). The fourth was given "Primolut N" until the pregnanediol excretion had fallen from the critical to the non-pregnant level. Ethisterone was then substituted and the pregnanediol excretion level corrected (Figure XIX).

Five patients had abortions in the pregnancy under investigation. This was surprising, since the pregnanediol level of three of them was corrected. In two of these

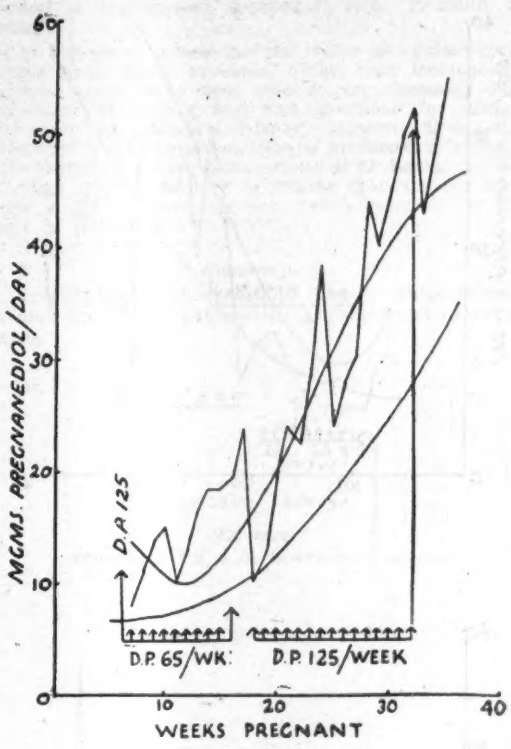

FIGURE XIII.
Previous abortions at 14, 18 and 12 weeks.

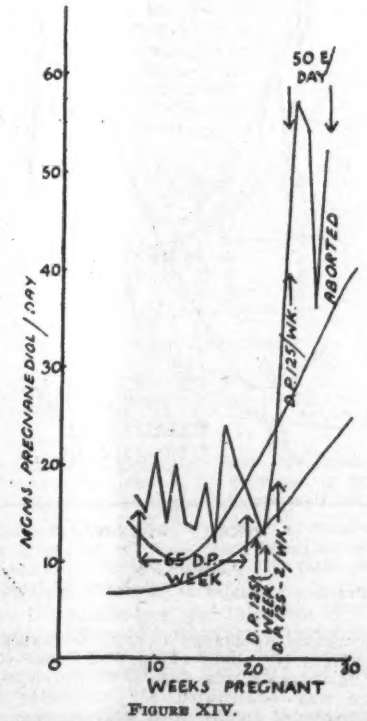

FIGURE XIV.
Previous abortions at 29, 21, 18 and 19 weeks.

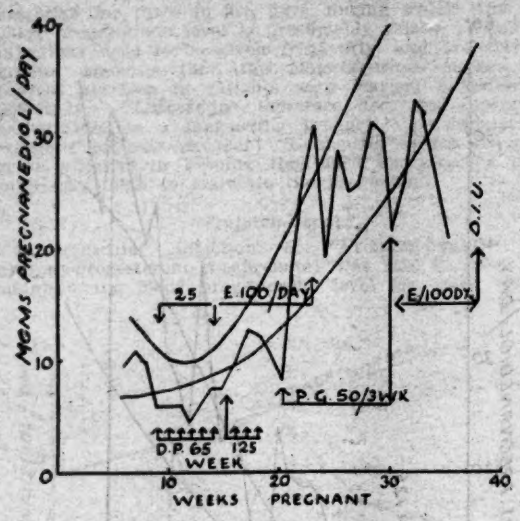

FIGURE XV.
Previous abortions at 39, 6, 9 and 10 weeks.

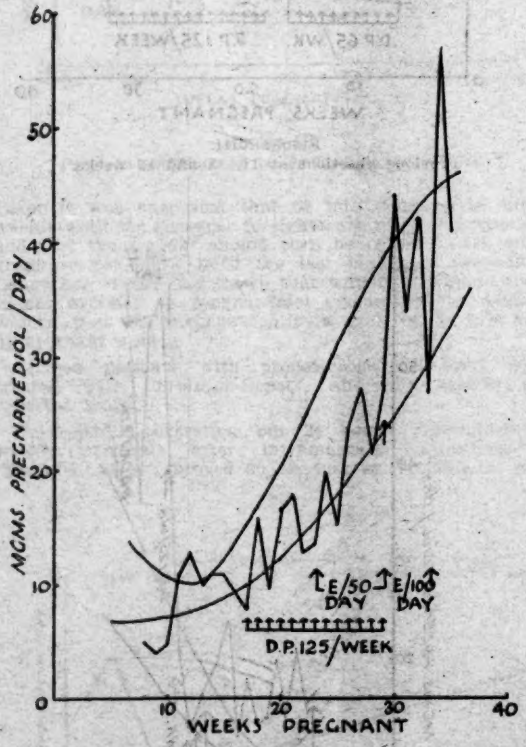

FIGURE XVI.
Previous abortions at 13 and 22 weeks.

cases the increased pregnanediol excretion appeared to be due to "Primolut N" alone (Figures XX and XXI). In the third the increase was due to "Proluton-Depot", and progesterone was substituted for "Primolut N" when abortion threatened while the patient was receiving "Primolut N" alone (Figure XXII). Two patients were

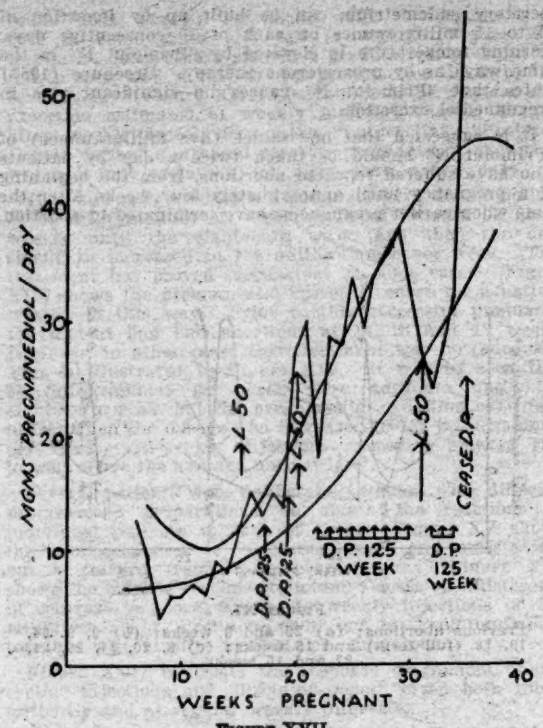

FIGURE XVII.
Previous abortions at 27, 9, 6, 8 and 18 weeks.

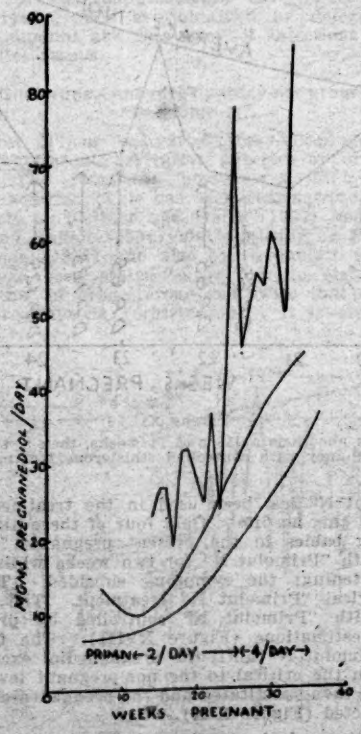

FIGURE XVIII.
Previous abortions after a full-term pregnancy at 8, 8, 8, 8 and 13 weeks.

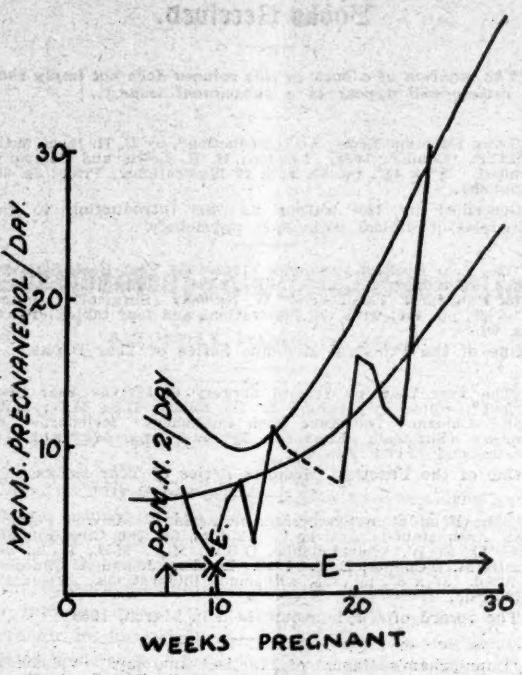

FIGURE XIX.
Previous abortions at 8 and 18 weeks. Pregnancy to 40 weeks with controlled ethisterone treatment.

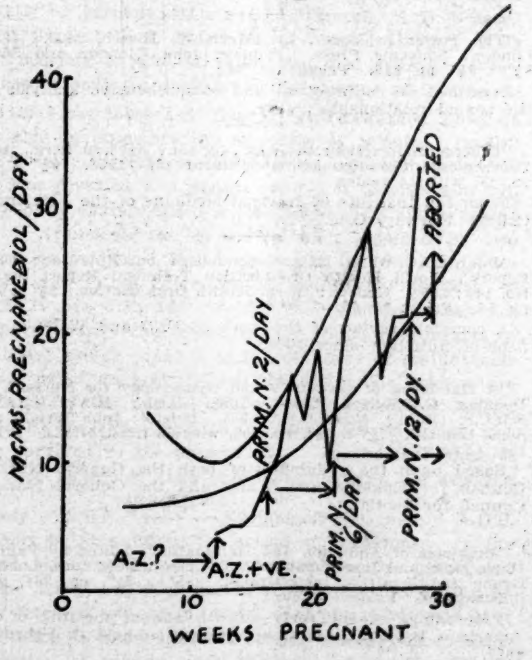

FIGURE XX.
Previous abortions at 26, 12, 6 and 8 weeks.

empirically treated. One of these, after two abortions at 21 and 22 weeks, had a full-term successful pregnancy with controlled ethisterone treatment, but had another abortion in the present pregnancy with "Primolut N" therapy.

It is difficult to assess the real value of "Primolut N" in this small series of cases. The high incidence of abortions could have been due to an unusually high proportion of patients who had abortions for reasons other than progesterone deficiency. However, it is established that pregnanediol excretion is increased in response to the ingestion of adequate amounts of "Primolut N"; but the claim that its activity is greater than that of ethisterone is not supported by the results reported for this aspect of its action.

Summary.

1. Progesterone implants fail to raise or maintain pregnanediol excretion significantly in progesterone-deficient women.

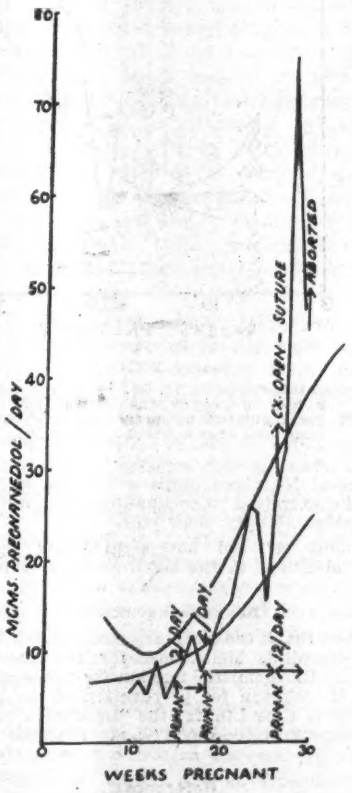

FIGURE XXI.
Full-term pregnancy and then abortions at 22, 15, 17 and 8 weeks.

2. Ingestion of "Lutocyclin" and "Proluton-Depot" by pregnant women is followed by increase in pregnanediol excretion. However, the results appeared very variable.

3. Pregnanediol excretion reaches a maximum about four days after the intramuscular injection of either of these progesterone preparations. It falls to the pre-injection level by the seventh day.

4. The earlier suggestions that injections of "Lutocyclin" or "Proluton-Depot" would maintain a raised progesterone level for three weeks have been disproved. Injections at least once per week are necessary for progesterone-deficient patients.

5. Pregnanediol excretion tests are a satisfactory guide to the treatment required by individual patients.

6. Injections of "Proluton-Depot" (125 milligrammes) are more effective than "Lutocyclin crystules" (50 milligrammes).

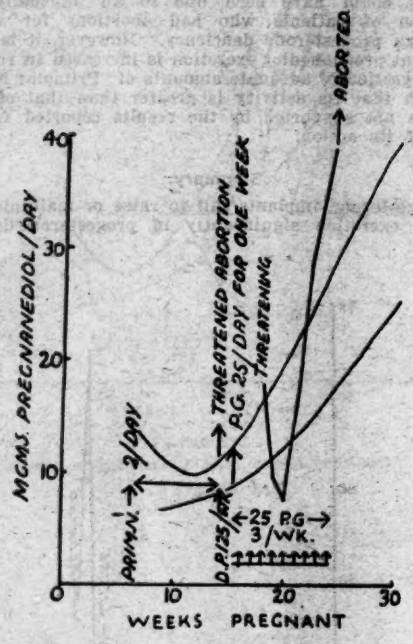

FIGURE XXII.

Previous abortions at 12, 14, 13 and 23 weeks. In this last pregnancy the patient had progesterone regulated by pregnanediol excretion tests and also a blood transfusion.

7. "Primolut N" given orally stimulates an increase in pregnanediol excretion in pregnant women, but it does not exhibit greater activity than ethisterone.

8. "Primolut N" did not significantly decrease the number of abortions in the small series of patients tested.

Acknowledgements.

We wish to thank the honorary medical staff of the Royal Women's Hospital, Melbourne, for the use of clinical material, the Biochemistry Section for technical assistance, and Miss M. Johnson for preparation of the graphs. We are indebted to Ciba Ltd. for the "Lutocyclin", and to A. G. Schering for "Proluton-Depot" and "Primolut N" used in this work.

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TULLNER, W., and HERTZ, R. (1953), "High Progestational Activity of 19-nor-progesterone", *Endocrinology*, 52: 359.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Lung Function Tests: An Introduction", by B. H. Bass, M.D., M.R.C.P. (Lond.); 1958. London: H. K. Lewis and Company, Limited. 7¼" × 4½", pp. 80, with 17 illustrations. Price: 8s. 6d. (English).

Described by the author as "an introduction to the principles of clinical pulmonary physiology".

"The Year Book of Pediatrics (1958-1959 Year Book Series)", edited by Sydney S. Gellis, M.D.; 1958. Chicago: The Year Book Publishers. Melbourne: W. Ramsay (Surgical), Limited. 7¾" × 5", pp. 496, with 123 illustrations and four tables. Price: 32s. 6d.

One of the Practical Medicine Series of Year Books.

"The Year Book of General Surgery (1958-1959 Year Book Series)", edited by Michael E. De Bakey, B.S., M.D., M.S.; 1958. Chicago: The Year Book Publishers. Melbourne: W. Ramsay (Surgical), Limited. 7¾" × 5", pp. 592, with 149 illustrations. Price: 32s. 6d.

One of the Practical Medicine Series of Year Books.

"Ciba Foundation Symposium on Amino Acids and Peptides with Antimetabolic Activity." Editors for the Ciba Foundation: G. E. W. Wolstenholme, O.B.E., M.A., M.B., B.Ch., and Cecilia M. O'Connor, B.Sc. 1958. London: J. and A. Churchill, Limited. 8" × 5", pp. 298, with many illustrations. Price: 45s. (English).

The record of a symposium held in March, 1958.

"Cunningham's Manual of Practical Anatomy." Volume II: "Thorax and Abdomen." Revised and edited by James Couper Brash, M.C., M.D., D.Sc., LL.D., F.R.C.S. (Ed.), F.R.S.E. Twelfth Edition; 1958. London: Oxford University Press. 7¾" × 5", pp. 594, with 237 illustrations. Price: 51s. 6d. (English).

The previous edition appeared in 1948.

"The Power to Love", by Edwin W. Hirsch, M.D.; 1958. London: Souvenir Press. Sydney: John Gilmour and Sons. 8½" × 5½", pp. 318. Price: 31s. 6d.

Described as "a practical and comprehensive analysis of the sexual relationship".

"Tuberculin Reactions in Dogs", by Olav Asbjørn Berg. *Acta Tuberculosea Scandinavica*, Supplement 43. 1958. 9½" × 6", pp. 48, with 14 tables.

From the Institute of Internal Medicine of the Veterinary College Norway, Oslo.

"Joint FAO/WHO Expert Committee on Nutrition: Fifth Report", World Health Organization Technical Report Series, No. 149; 1958. Geneva: World Health Organization. 9½" × 6½", pp. 55. Price: 3s. 6d.

A complete review of the work of FAO and WHO in the field of nutrition since 1954.

"A Handbook of Obstetrics and Gynæcology for Nurses", by Douglas G. Wilson Clyne, B.M., B.Ch., M.A., L.R.C.P., F.R.C.S. (Edin.), M.R.C.O.G.; 1958. Bristol: John Wright and Sons, Limited. 7¼" × 4½", pp. 208, with 53 illustrations. Price: 15s. (English).

Based upon the syllabuses of both the General Nursing Council for England and Wales and the General Nursing Council for Scotland.

"Problems of Addiction and Habituation", edited by Paul H. Hoch, M.D., and Joseph Zubin, Ph.D.; 1958. New York, London: Grune and Stratton, Incorporated. 8½" × 5½", pp. 264, with illustrations. Pridce: $6.50.

Proceedings of the forty-seventh annual meeting of the American Psychopathological Association held in February, 1957.

"Pædiatrics for the Practitioner: Supplement 1958." Under the general editorship of Wilfrid Gaisford, M.D., M.Sc., F.R.C.P., and Reginald Lightwood, M.D., F.R.C.P., D.P.H.; 1958. London: Butterworth and Company (Publishers), Limited. 9½" × 6½", pp. 156, with five illustrations. Price not stated.

The third supplement to "Pædiatrics for the Practitioner".

The Medical Journal of Australia

SATURDAY, MARCH 28, 1959.

THE CHANGING FACE OF DIABETES.

UNTIL recently it was relatively easy to give a brief and coherent account of the relevant biochemical background of diabetes. The story was that deficiency of insulin prevented the customary disposal of carbohydrate, which in consequence accumulated in blood and tissue, spilling over into the urine. The body was forced to look elsewhere for its immediate energy requirements and sooner or later made such extravagant use of fat as to allow the accumulation of waste products of lipoid metabolism in harmful concentrations. Elaboration of this theme was about as far as one could go. Recent advances in biochemistry, of which useful accounts have been published recently by various authors (G. G. Duncan,[1] S. B. Beaser,[2] W. C. Stadie,[3] V. P. Dole[4]), have changed all this; it is now possible to give a fuller, but not always clearer, picture of body metabolism in the absence of insulin.

In 1956 the labours of Sanger were rewarded when he was able to announce the structure of insulin. Insulin thus became the first protein hormone of which the structure was revealed, and Sanger showed it to consist of two polypeptide chains, called A (composed of 21 amino acids) and B (composed of 30 amino acids), joined by two disulphide bridges. The A chain has its own disulphide bridge, and in all there are 51 amino acid residues, of which 16 are different. So far this knowledge has not helped to clarify the mechanism by which insulin acts in the body; minor changes in the sequence of amino acids do not affect its activity, but the disulphide bridges are essential for the normal action of the hormone. Among the many theories suggested to account for its action, two have survived to the present time. In the first place it has been suggested that insulin encourages the reaction

$$\text{Glucose} + \text{A.T.P.} \xrightarrow{\text{hexokinase}} \text{Glucose-6-phosphate} + \text{A.D.P.}$$

probably by stimulating the action of hexokinase. In the second place, insulin appears to promote the passage of glucose across cell membranes, in this way facilitating its entry into the cells of the body. Recent experiments have done much to show that the second theory best explains the action of insulin upon the cells of muscle, but in relation to the liver the first theory is more in accord with observed facts. The liver cells of diabetic rats show the following metabolic abnormalities: (i) diminished uptake of glucose, (ii) diminished oxidation of glucose to carbon dioxide, (iii) diminished conversion of glucose to glycogen, (iv) diminished ability of liver cells to phosphorylate glucose, and (v) increased formation of glucose from non-carbohydrate precursors. It is therefore likely that a metabolic block occurs in the early stages of glucose metabolism, but there is no change in the permeability of liver cells to glucose. The probable site of this metabolic block is at the level of hexokinase activity. A further difference between the action of insulin upon the cells of muscle and those of liver is seen in the phenomenon called metabolic adaptation. The action of the hormone upon muscle is almost instantaneous (within one minute). In the diabetic rat, on the other hand, insulin requires from six to twenty-four hours before complete restoration to normal of the metabolism of the liver cells is achieved. This latent interval has been a source of considerable interest; some workers have suggested that the time is occupied in the synthesis of some protein enzyme or co-factor required to complete an enzyme system which in the absence of insulin has lost its function. Studies of the metabolism of adipose tissue in the absence of insulin show certain similarities to that of the liver, while in brain no demonstrable change has been detected. In other tissues experimental studies have been too few to lead to definite conclusions.

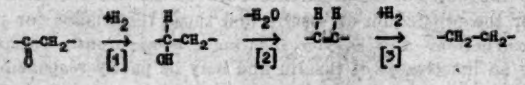
Inhibitors of insulin have recently been studied in great detail. The ultimate activity of insulin must be regarded as the outcome of a balance between factors responsible for the production of insulin and those responsible for its destruction. The enzyme insulinase is apparently specific as an inactivator of insulin and may be partly responsible for the short half-life of injected insulin (about thirty-five minutes). In addition, at least five factors have been identified in the blood which inhibit carbohydrate metabolism at one point or another. The first of these inhibits the basal uptake of glucose by rat diaphragm and occurs in poorly treated alloxan-diabetic rats. It is found in the lipoprotein fraction of serum with beta and gamma globulin, is dependent on the presence of the adrenal and pituitary glands, and is produced by their hormones in non-diabetic subjects. The second inhibits increased uptake of glucose by rat diaphragm following the addition of insulin. It occurs in the poorly treated alloxan-diabetic rat and in persons with untreated diabetes. It is found in the beta globulin of serum and is dependent on the presence of the adrenal and pituitary glands. The third inhibits extra glycogen synthesized by rat diaphragm under the influence of insulin and is associated with diabetic coma. It is found in the alpha globulin of serum. The fourth inhibitor is an insulin antibody. It is associated with severe diabetes treated with insulin and is found in the gamma globulin of serum. The fifth is also an insulin antibody. It is associated with insulin-resistant diabetes and is found between the beta and gamma globulin of serum. Of these five factors, the last three are possibly important clinically.

Like insulin, glucagon has recently been closely studied. Its structure is known; it is a protein, and is secreted by the alpha cells of the pancreas. Early experiments seemed to indicate that the secretion of glucagon was stimulated by growth hormone, but this now seems unlikely. The

[1] *Bull. N.Y. Acad. Med.*, 1958, 34: 73.
[2] *New Engl. J. Med.*, 1958, 259: 525.
[3] *Bull. N.Y. Acad. Med.*, 1958, 34: 5.
[4] *Bull. N.Y. Acad. Med.*, 1958, 34: 21.

hormone causes a rise in blood sugar level by promoting the conversion of glycogen to glucose in the liver. The site of this action is believed to be upon phosphorylase, the glycogenolytic enzyme of liver. In addition to its action in the liver, glucagon has been shown to enhance the peripheral utilization of glucose, and for this reason should not be regarded as an insulin antagonist. In fact, the two hormones increase the utilization of glucose to a greater extent than either hormone alone; acting in concert, they are capable of exerting a finer regulatory action upon blood glucose levels than insulin alone. The secretion of glucagon is controlled by the blood level of glucose, being depressed by a rise in blood glucose level and vice versa, and by direct action of glucagon itself upon the alpha cells of the pancreas.

Although fatty acids are oxidized in the usual way in diabetes, the disease is commonly accompanied by three abnormalities of fat metabolism: (i) the synthesis of fatty acids is impaired; (ii) the mobilization of fat from tissue stores is increased; (iii) lipoids accumulate in abnormal quantities in various tissues. We shall consider these three in turn. After a period of fasting, changes in fat metabolism like those seen in diabetes appear, only to be reversed after the ingestion of carbohydrate. It is known that this phenomenon is due to the coupling of fatty acid synthesis with the oxidative changes in the tricarboxylic acid cycle. It has recently been possible to show that in diabetes a block occurs in the synthesis of fatty acids. During this synthesis the following steps occur:



The second step requires a strong reducing agent, which acts in conjunction with the oxidation of iso-citrate, and it is at this point that the synthesis of fatty acids is interrupted during fasting and in diabetes. A block to fat synthesis at this point contributes to the accumulation of ketone bodies. Turning to the second abnormality, the increased mobilization of fat from tissue stores, we find that the non-esterified fatty acid of normal plasma (NEFA) is low in concentration, but is capable of extremely rapid turnover, which enables it to act as the principal agent in the mobilization of fat from depots. The concentration of plasma NEFA is high in diabetes and shows a sharp rise before the onset of ketosis, as, for example, when an unstable diabetic misses his morning insulin. There is indirect evidence to show that a rise in plasma NEFA content is associated with an increase in the flow of fatty acids from blood to liver and other organs. Moreover, it has been calculated that a simple block in the synthesis of fatty acids without a fall in the rate of hepatic oxidation or a rise in the amount of substrate delivered to the liver could not lead to ketosis of the severity seen in diabetic coma. It is likely that a relative deficiency of oxalacetate (i.e., relative to the amount of substrate offered to the liver) may result from uncontrolled discharge of NEFA from fat depots, which, in consequence, flood the liver with fatty acid precursors such as acetate; the concomitant defect in fat synthesis already mentioned has the effect of exaggerating this accumulation of acetate. When a normal liver is flooded with fatty acids, this results in a fivefold increase in the production of ketone bodies without impairment of fatty acid synthesis. The third abnormality is the deposition of lipoids. It is possible that the excess of fatty acid precursors (acetate and acetoacetate) accumulating in the liver in the manner described may push the disposal of acetate in other directions, such as towards the synthesis of cholesterol. In this way the excessive mobilization of fatty acids in diabetes may contribute to the production of chronic cumulative lesions, such as xanthomata and arteriosclerosis.

Phosphate metabolism in diabetes is also of interest. Just as the Krebs cycle is linked with the synthesis of fatty acids, so also is it linked with the metabolism of inorganic phosphate, since certain metabolites of the cycle normally incorporate phosphate into organic compounds of high energy content; for example, adenosine triphosphate and such compounds are the source of chemical energy for a number of important metabolic activities. This process, called oxidative phosphorylation, occurs exclusively in mitochondria, and it has been shown that the mitochondria of liver cells are unable to institute this type of phosphorylation at a normal rate in animals made diabetic by pancreatectomy; this defect is remedied by treatment with insulin. Impairment of oxidative phosphorylation is thought to be an important factor in the abnormal metabolic activities of diabetes.

To sum up, we may say that present trends in biochemical research into the subject of diabetes lean more and more towards the subject of fat metabolism. Recent advances in the study of fat synthesis have enabled biochemists to unravel the mysteries of lipoid metabolism in diabetes, but during this process of exploration the picture presented seems more confused than ever. Nevertheless, we are probably closer to understanding the occurrence of abnormal lipoid metabolism in apparently well-controlled diabetics.

Current Comment.

MAIMONIDES AND MEDICINE.

Rabbi Moses ben Maimon was born on March 20, 1135, in Cordoba, which city, though somewhat past its brilliant prime, was still one of the great centres of enlightenment in the Islamic world. In 1188 Cordoba came into the power of the Almohades, a fanatical sect, and the previous freedom of Jews came to an end. The young Moses was taken to Fez, where he spent five years in the study of literature and philosophy. In 1163 the family left for Egypt, and it was during his early stay here that through a shipwreck he lost all his capital and was forced to seek some means of livelihood. He chose medicine and soon became renowned throughout the civilized world as a great physician, being appointed body doctor to the famous Saladin. The theological and philosophical writings of Maimonides have given him a high place amongst the world's thinkers; Hebrews like Spinoza and Christians like Aquinas have been deeply influenced by his works, whilst amongst Hebrews of today he occupies a position second only to Moses the prophet. But little attention has been given to his contribution to medicine. "More theologian and more philosopher than doctor" was a mediæval verdict which has been retained.

Enrique Schorr[1] has recently published an article entitled "*Maimonides Medico*" which gives a balanced account of the position of the great Rabbi in the history of medicine. Though he was no Galen, he was yet outstanding in his practice and in his writings. Asthma, *poisons and their antidotes, hæmorrhoids, diet and baths* are some of the subjects dealt with. In certain respects he was a true pioneer. Thus he vigorously championed hygiene. Here are some of his aphorisms on this topic: "The principal aim of medicine is not so much the cure *of diseases as their prevention.*" "*One should hold the* view that medicine is a science very necessary for humanity at all times and in all places, not only in *illness but in health.*" "*Out of every thousand men only* one dies a natural death, the others are victims of ignorance or vice." Perhaps his greatest contribution to medical theory and practice was in the realm of psychotherapy. As an Arab poet put it: "The art of Galen was *concerned with the cure of the body, that of* Maimonides with the cure of body and mind." His advice to disciples was: "Study each causal factor and *treat it; treat each psychic condition for even if it is* not causal it can influence the progress of disease. Treat psychic conditions irrespective of whether or not they are apparently associated with disease."

Maimonides, like all great doctors in history, believed *in a few ideas which are now considered to be false.* Just as John Wesley, who is still revered by many of his followers as a physician, insisted on the existence of demonic possession and held disbelief in witchcraft as blasphemous, so Maimonides stoutly upheld the practice of venesection and placed great emphasis on the "buffy coat" as a causal factor and not as a consequence of disease. However, he was a great man, and this *sympathetic study from another angle than that usually* adopted is welcome.

A NATIONAL BIOLOGICAL STANDARDS LABORATORY.

An interesting announcement was made by the Commonwealth Minister for Health, Dr. Donald Cameron, *during the Address-in-Reply to the Governor-General's* speech in the House of Representatives on February 18, 1959. Referring to certain important developments in the field of health, Dr. Cameron stressed the importance of biological products and mentioned the developments *that had taken place in the Commonwealth Serum* Laboratories, which are part of the Commonwealth Department of Health. He then went on to say that *it was important, not only to have a supply of such* substances, but also to ensure that, just as there were standards of accuracy in other fields such as weights and measures, and just as there were standards of purity, potency, safety and effectiveness required with *regard to what he might roughly describe as inorganic* medicines, the ordinary pharmaceutical preparations, so it was important that there should be national standards and facilities for testing all the biological products that were used in Australia. It would be realized that the setting up of such standards required in the first place highly skilled personnel, and in the second place a first class laboratory and facilities for those persons. Dr. Cameron thought that it was important, or at any rate highly desirable, that the laboratory should be located in the national capital. Accordingly the Government had taken steps to set up a National Biological Standards Laboratory in Canberra. Its establishment was now going on, the responsibility for it being that of the Department of Health.

Dr. Cameron then went on to refer to the functions of the laboratory. Apparently it is first of all to act as an agent for the Director-General of Health in the examination of goods referred to it—that is, goods containing a therapeutic substance. Secondly, it is concerned with the testing of new therapeutic substances. *Thirdly, it has to provide expert advice to the Depart*ment of Health on such matters, and also of course to the medical profession and to other persons concerned. Fourthly, it has to prepare, distribute and keep Australian national standards of biological and pharma*ceutical preparations, and to collaborate with other* laboratories in the establishment of new international standards. Dr. Cameron announced that the services of a highly skilled medical scientist had been obtained to act as director of the laboratory, and with the coopera*tion and assistance of the Australian National University,* buildings had been secured in which the laboratory would commence to function in the very near future.

This development is, as Dr. Cameron commented, a matter of immense scientific importance to medicine and *health in Australia. It will be of great interest to see* just how extensive will be the field covered by this laboratory. Wisely used, it could serve, not only to *maintain and raise still higher the standard of the best* biological products available in Australia, but also to eliminate anything inferior which might tend to creep in. There is a real need for the control of standards of therapeutic substances in general. This new measure *should take care of biological substances. Perhaps some*thing constructive now can be done in the wider, and admittedly more difficult, field to ensure that therapeutic *substances supplied to the medical profession and the* general public, and especially those supplied free, shall be of uniformly high standard.

[1] *Arch. esp. Med. interna*, 1958, 4: 317.

CELLULAR PATHOLOGY.

It is now one hundred years since Rudolph Virchow inaugurated the new era of cellular physiology and *pathology with the publication in 1858 of his work on* cellular pathology. Although he taught that all cells originate from pre-existent cells and that the cell is the fundamental unit of disease, the emphasis, until recently, has been upon histological morphology. Lately, however, there has been a great stimulus to cytological research through the advent of new techniques such as electron microscopy, histochemistry and the use of *radioactive isotopes. In order to commemorate this* significant centenary, the Royal College of Surgeons held a symposium on October 2, 1958. The participants in the symposium are all notable for their interest in the cell, and their contributions surveying a wide field *of present-day developments in cellular physiology and* pathology are published in *The Journal of Clinical Pathology* of November, 1958. The morphology of the *cell as revealed by the light microscope has assumed* great importance in the recognition of cancer cells in body exudates, and the history of this development is presented by J. Bamforth and G. R. Osborn. However, as one reads the papers in this symposium, one sees that *it is the submicroscopic structure which is the important* field of the future. In the words of the chairman of the symposium in his summing-up: "When we speak of the cell, which is so small, we should at the same time realize that it is large enough to encompass all groups of workers in pathology. Indeed, when we speak of the cell, we are speaking of pathology as a whole." There is an interesting account of the structure of the bacterial cell by Robert Cruikshank, and the fascinating story of tissue culture is related from first-hand experience by Honor Fell. J. W. Harman, in his paper on cytochondrial aspects of cellular pathology, illustrates the pursuit of the disease processes to subcellular levels. One might say that a morphology of metabolism is emerging, and in the paper by A. G. Everson Pearse this idea is reinforced. He shows how histochemistry has extended the limits of cellular pathology to the sites of enzyme activity. As our knowledge of the cell increases, so our concepts of humoral and organ pathology are being replaced by discoveries at the subcellular and enzyme level. Many disciplines contribute to this knowledge, but they all derive from the unifying concept of Rudolph Virchow.

Abstracts from Medical Literature.

SURGERY.

Peptic Ulcer after Sixty.

C. W. Cutler, junior (*Surg. Gynec. Obstet.*, July, 1958), reviews the clinical patterns of peptic ulcer in patients more than 60 years of age, as exemplified by 430 cases of peptic ulcer in such patients recorded at the Roosevelt Hospital between 1940 and 1955. These comprised nearly one-fifth of all ulcer patients admitted during this period. The average age of these patients was 66·4 years, and three-quarters of them were men. The location of the ulcer was duodenal in 286 of these cases, gastric in 126, both duodenal and gastric in eight, and marginal in 11. During the same period 176 patients over 60 years of age were admitted to the hospital with cancer of the stomach. It was noted that in relatively few cases had ulcers developed for the first time after the age of 60 years, but those ulcers that did so often manifested themselves by severe hæmorrhage or perforation, preceded by symptoms of short duration or no previous complaints. In the whole series the most frequent emergency complication was hæmorrhage, and in a fair proportion of these cases bleeding had occurred before. The second most frequent serious emergency was perforation, and this usually occurred in chronic cases of long standing, less frequently as the result of late-developing ulceration. Patients with pyloric obstruction almost all had long-standing ulcer complaints. The largest group of patients was those with symptoms of many years' duration who sought relief from the intractability of their ulcers. It was found that in many cases of hæmorrhage surgical intervention was necessary, and, if the patient's condition was favourable, subtotal gastrectomy was successfully undertaken in a large proportion of cases. Surgical intervention was also necessary in cases of perforation, but in this age group simple closure was considered the safest procedure. In cases of obstruction and of intractability, a less hazardous procedure than subtotal gastrectomy was preferred unless cancer was seriously suspected, except when the patient was in good condition. Finally, the author points out that in all groups, except those with perforation, medical as opposed to surgical measures have much to recommend them and are successful in many cases; he also states that general conclusions are futile and that each case is a distinct problem in itself.

Cancer of the Stomach after Resection for Peptic Ulcer.

R. Côté, M. B. Dockerty and J. C. Cain (*Surg. Gynec. Obstet.*, August, 1958) describe 17 cases, recorded in the files of the Mayo Clinic, in which cancer of the stomach has developed after excisional operations for peptic ulcer. In five of these the patient had undergone gastric resection, and in 12 the patient had been treated by local excision of the ulcer, usually accompanied by gastroenterostomy. Twelve of the patients had gastric ulcers and five had duodenal ulcers. The authors state that the small number of cases found during a 50-year period at the Mayo Clinic leads them to believe that cancer of the stomach rarely develops in patients who have been treated for peptic ulcer either by gastric resection or by excision of the ulcer.

Hypothermia with Intragastric Cooling.

M. H. Holt, R. Benvenuto and F. J. Lewis (*Surg. Gynec. Obstet.*, August, 1958) state that the present technique for inducing hypothermia in surgery is not completely satisfactory. They describe their experience in the use of an intragastric device through which a constant volume of water is circulated at a controlled temperature, and which can be used in conjunction with thermal blankets to control the temperature of a patient during an operation. Experiments with dogs were satisfactory, and histological examinations of the gastric mucosa of dogs subjected to temperatures ranging from 65° C. to 3° C. showed no damage. The apparatus was then used on six patients, three of whom were undergoing a heart operation and three a neurosurgical operation. It was found that the intragastric device, in conjunction with thermal blankets, reduced the cooling time by almost one-half and the rewarming period by one-fifth. Clinical observations and laboratory studies demonstrated no alteration of gastric function. The intragastric device proved to be especially useful in situations in which the body contact with blankets was limited because of special positioning of the patient. The authors state that the apparatus is simple to assemble and operate, and occupies little space in the operating room.

Pneumatosis Intestinalis.

Z. Mujabed and J. A. Evans (*Surg. Gynec. Obstet.*, August, 1958) review the clinical, pathological and radiological features of pneumatosis intestinalis (gas cysts of the intestine). They state that the condition is an uncommon disease of the gastro-intestinal tract in humans, but is a not uncommon finding in lower animals, especially pigs. It is characterized by the presence of loculated collections of gas in the walls of any part of the gastro-intestinal tract or in the mesenteries. It may be found in all age groups. The authors describe seven cases, of which four were in babies, all of whom had intractable diarrhœa, and all of whom came to autopsy; two had ulcerations through which gas might have dissected into the walls of the intestine. In adults the condition is frequently asymptomatic, and is revealed at autopsy or as an unsuspected finding on X-ray examination; the cysts are associated with gastric or duodenal ulcer in approximately 50% of such cases.

Burns in Casting Foundries.

R. G. Main (*Brit. J. Surg.*, September, 1958) studied the burns occurring in moulders in light casting foundries. Minor burns from sparks are treated at the works ambulance room without loss of working time. Men with burns which are rather more severe, but under one inch in diameter, are treated in the casualty department of a hospital as out-patients, but those with still more severe burns require admission to hospital. The records of 37 such in-patients were studied. The burns, on the whole, were not extensive; burn shock was not a problem; fluid loss or shift was slight, and intravenous infusion was rarely required. The lower extremities were almost exclusively involved, the burns being mainly confined to the foot and ankle. Full-thickness skin loss occurred in nine out of every 10 cases, and skin grafting was performed on nine of the 37 patients. Most burns were caused by molten metal, which was being carried in a ladle to the mould, spilling on to the patient's leg and running into his boot. Sometimes the burns resulted from the bursting of a "box", which is filled with molten metal, and very occasionally a moulder might be trapped in a pool of molten metal when a large leak had occurred. The traditional method of conservative treatment and later skin grafting resulted in an average period of hospitalization of 50 days. After a change in policy was instituted, the burns were excised and skin grafts applied, or if possible the defect was sutured, as an emergency measure, within 24 hours of injury. With this policy the average period of hospitalization fell to 25 days. Recommendations are made for ways of preventing these accidents.

A New Intestinal Bactericide.

J. F. Connell and L. M. Rousselot (*Surgery*, September, 1958) report studies on a new antibiotic, framycetin sulphate ("Soframycin"), for use in intestinal surgery. They found that the drug is minimally absorbed when taken by mouth and is non-toxic, no untoward effects being noted on any system. They found that suppression of bacteria was rapid in the non-obstructed colon with comparatively low doses. Three grammes per day for 48 hours was the optimal dose for adequate control, which they state is about half the dose required for neomycin. They noted also that few yeast colonies appeared on the 48-hour bowel preparation. Thus no supplemental drug, such as nystatin, was required.

Chronic Regional Enteritis.

B. B. Jackson (*Ann. Surg.*, July, 1958) presents a study of 126 cases of regional enteritis treated at the Massachusetts General Hospital from 1937 to 1954. There was involvement of the colon in 43%, involvement of the distal 15 to 20 cm. of ileum in 44%, and skip areas were present in 25%. Indications for surgery were considered to be the complications of the disease, namely hæmorrhage, obstruction, perforation, fistula formation and the presence of a right lower quadrant mass; this last finding was interpreted as evidence of an internal fistula or partial obstruction. Surgery was performed in 104 cases; there were four deaths among 86 patients treated by resection and four deaths among 57 patients treated by short-circuiting operations. If the lesion is localized and can be excised safely and the patient's condition permits, resection is preferred; otherwise a short-circuiting operation with complete division of the bowel is indicated. In regional enteritis the appendix may be excised safely only if

the ileo-cæcal junction and 30 cm. of adjacent ileum are normal. The drainage of an abscess related to affected loops of bowel frequently led to fæcal fistula. Intractable ano-rectal complications are most satisfactorily handled by a permanent sigmoid colostomy. The follow-up period ranged from two to 26 years. Resection gave good results in 60% of 86 operations. Excisions of the terminal part of the ileum and right half of the colon had the best prognosis when the disease was confined entirely to this region. Short-circuiting operations with complete transection of the bowel gave good results in 52% of 48 operations. Patients may be free from enteritis for 15 to 20 years and then have a recurrence; on the other hand patients free from disease for more than four years may be permanently cured. It seems that chronic regional enteritis in people over 50 years old has a more benign course than in younger age groups.

Lumbar Sympathectomy.

W. C. RANDALL, W. J. PICKETT, F. A. FOLK AND H. J. MCNALLY (*Ann. Surg.*, July, 1958) discuss the effective level of lumbar sympathectomy. They stimulated various parts of the sympathetic trunk and rami communicantes electrically at operation, and recorded the sweat responses of the complete circumference of thigh, calf and foot by the iodine-starch-paper technique. About three weeks after the operation the sweat response was studied after heating the patient. The method was found to be a practical and valuable way of determining the levels of entry of preganglionic and exit of post-ganglionic fibres to the lower limb; it indicated at the time of operation the part of the trunk which had to be removed to denervate a given area of skin; and it was frequently useful in identifying tissue as sympathetic. Marked variations in the level of entry of the preganglionic pathways and in the distribution of the ganglia were found. Extensive denervation including the second to fifth, or even the first to fifth, lumbar segment was frequently needed to eliminate marked residual sweating after operation, and such procedures gave more satisfactory therapeutic results.

Overtransfusion in Massive Hæmorrhage.

J. W. DOWNS (*Ann. Surg.*, July, 1958) discusses the problem of circulatory overloading due to overtransfusion in cases of massive hæmorrhage, and describes four illustrative cases. The clinical picture is clearly established. During transfusion or within an hour of its completion the patient suddenly becomes dyspnœic, orthopnœic and intensely cyanotic. Blood-tinged frothy sputum may be coughed up. The venous pressure is elevated, as indicated by engorgement of the jugular veins in the erect position. The lungs fill with sibilant and sonorous râles, and auricular fibrillation may occur. The patient may die within a few minutes of the onset of symptoms, but the outcome depends on the degree of overloading and his ability to tolerate it. If the patient survives for some hours, peripheral œdema may develop. The condition is an emergency, and delay of a few minutes may be fatal. Tourniquets are applied to all four extremities to occlude the venous return but not the arterial pulsations, and within five minutes the diagnosis should be confirmed by clinical improvement. Phlebotomy is performed, and the tourniquets are then removed and the patient is observed for further signs of over-transfusion; it may be necessary to withdraw more blood. Positive pressure oxygen therapy is helpful in combating marked pulmonary œdema and frequent tracheal aspirations are used to remove fluid accumulations. Fluids should be restricted so as to produce the minimum adequate urinary output, and should contain no electrolytes unless specific electrolyte deficiency exists. A temporary psychosis developed in the three surviving patients, and lasted from five to seven days.

Common Bile Duct and Major Pancreatic Duct Injuries During Operation.

J. C. CARPENTER AND W. B. CRANDELL (*Ann. Surg.*, July, 1958) report three cases of injury to both the main pancreatic and the common bile duct during operations for duodenal ulcer. From the literature they have gleaned 16 cases of injury to the common bile duct or duct of Wirsung, but suspect that this type of injury is more common than is generally appreciated. In the three cases described the injured ducts entered the first part of the duodenum. Such an abnormality may be due to scar contracture around an ulcer or congenital abnormality, but the former mechanism is considered responsible in the authors' cases. Methods of avoiding this injury are described: a probe may be placed in the common duct; any suspicious structure in the groove between the duodenum and the head of the pancreas may be aspirated; dissection for more than 1 to 2 cm. beyond the gastro-duodenal artery should be avoided; a two-stage operation may be adopted when the duodenal dissection is difficult; and before operation, intravenous cholangiography might be considered for patients with severe distortion of the pylorus. In the established injury, end-to-end anastomosis of the common bile duct was adopted in one case, but stones in the gall-bladder migrated into the common bile duct beyond the anastomosis and caused leakage; in the other two cases the ducts were successfully implanted into an isolated limb of jejunum.

Carcinoma of the Rectum.

J. M. WAUGH AND J. C. TURNER, JUNIOR (*Surg. Gynec. Obstet.*, December, 1958), review 268 cases of carcinoma of the rectum treated at the Mayo Clinic by combined abdomino-perineal resection with preservation of the external anal sphincter. The operations were performed by the senior author, using a modification of the Hochenegg "pull-through" procedure; in over 80% of these cases the lower border of the lesion was between 5 cm. and 10 cm. from the anal margin, most patients with a lesion in the distal 5 cm. being treated by the Miles procedure. In 43% of the cases regional lymph nodes were involved; in 10% the operation was regarded as palliative only, because metastases were present in the liver. The most frequent post-operative complications were urinary retention, presacral infection, and retraction or slough of the transplanted sigmoid. Nine patients died in the immediate post-operative period. Of the 155 patients who had been followed up for five years or longer, and in whom there were no hepatic metastases at operation, 86 (55%) had survived for five years; in the group without lymph node metastases 73% had survived for five years, but in those with lymph node metastases 27% had survived that long. Satisfactory continence of fæces resulted in 78% of cases. The authors consider that these figures bear out their contention that combined abdomino-perineal resection with preservation of the anal sphincter offers a rational method of treatment of carcinoma of the mid portion of the rectum, if it includes ample resection of the sigmoid mesentery, the perirectal tissue and the internal anal sphincter, and that the results compare favourably with those following the Miles operation.

Vascular Invasion in Bronchogenic Carcinoma.

H. T. LANGSTON *et alii* (*Surg. Gynec. Obstet.*, December, 1958) state that recent interest has been focused on the zones of lymphatic spread of bronchogenic carcinoma, and this has led to the development of a more radical operative procedure which is designed to incorporate total mediastinal lymph node removal along with pneumonectomy. However, direct vascular spread has secured less attention, but may be of great importance in determining survival of patients with this disease. In order to gain further information on the incidence of vascular invasion in bronchogenic carcinoma, the authors have utilized the cytological as well as the histological approach to study the specimens obtained from 15 patients treated surgically. These specimens were perfused, immediately after their removal from the chest, through blunt-tipped canulæ inserted into the pulmonary vein or veins. The pulmonary vein was then dissected and tissue sections were cut. The perfusion fluid was centrifuged and attempts were made to concentrate any malignant cells by means of the albumin flotation technique. In 12 out of 15 cases carcinoma cells were found in the perfusate. Of the three cases in which no carcinoma cells were found, in two vascular invasion was seen in the histological section. Thus in 14 of the 15 cases studied there was actual evidence of vascular invasion by the tumour.

Prevention of Air Embolism in Cardiac Surgery.

R. DE VERNEJOUL *et alii* (*Presse méd.*, November 22, 1958) have studied experimentally a technique for the prevention of air embolism of the coronary artery during operations on the left side of the heart. They have found that intra-coronary injections of carbonic acid gas are much less dangerous than air embolism. They describe a technique by which the pleural cavity is filled with carbonic acid gas during the opening of the heart, so that, if there is a gas embolism, the bubbles of carbon dioxide will be rapidly eliminated.

British Medical Association.

NEW SOUTH WALES BRANCH: SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held on November 27, 1958, at the Robert H. Todd Assembly Hall, B.M.A. House, 135 Macquarie Street, Sydney, DR. A. W. MORROW, the President, in the chair.

Wound Infection.

DR. R. W. D. MIDDLETON read a paper entitled "Wound Infections" (see page 426).

DR. H. L. CARRUTHERS read a paper on wound infection. This paper has not been made available for publication.

DR. C. C. MCKELLAR said that it was most regrettable that such an important subject should have produced only a very small audience, and apologized for having failed to bring along figures which were available for one of his own hospitals. However, he hoped to compensate by asking a lot of questions. He would particularly like to obtain some world figures for infection in the world's best centres, but with specified definition of infection and of manner of selection, if any, of the cases quoted. He had failed to obtain such figures from the "Any Questions" of the *British Medical Journal*.

Dr. McKellar asked for a comment on the supply of unsterilized water for "scrubbing up", which had without notice been supplied to one hospital; he understood that it was now Hospital Commission policy. The next question was what to do about the badly wanted instrument which had been dropped on the floor during an operation. He also asked what was the approved procedure for dealing with instruments after operation on an infected subject. With respect to masks, he was pleased to hear Dr. Middleton's recommendation that they be changed after each operation. He asked for further evidence of the necessity of that procedure which could provide ammunition for requesting the large supply of masks required from a hospital matron or secretary.

Dr. McKellar finally expressed the hope that there would be continued development of the plan for cooperation between infection committees in each hospital with the central advisory committee on hospital infections of the New South Wales Branch of the British Medical Association.

DR. DAVID FAILES said that at Sydney Hospital, over the past five years, an intensive investigation had been conducted into wound infection. It had been their practice to investigate each year all "clean" operations; if a wound showed any discharge, a swabbing was taken for bacteriological analysis. A wound was regarded as being infected if it discharged pus, or if it discharged serum or fluid from which a pathogen could be cultured. Surveys had been carried out on all "clean" operations conducted over the whole of the period 1954-1955, for three months in 1957 and for four months in 1958. An over-all incidence of infection of the order of 7% was found in 1954; for the first three months' period it was 10%, for the second 11·5%, for the third 9%, and for the last only 1·5%. The marked reduction in infection during the last three months of the year was due to an intensive effort by all members of the hospital staff to eliminate every possible avenue of infection. In 1955, the incidence for the first six months was 4%, and for the second six months 4·5%. In the first three months of 1957 the incidence was 7·1%; in the first four months of 1958 it was 6·4%. Thus the average over-all incidence had been of the order of 6% to 7%.

Dr. Failes said that it was easy to keep statistics, but not to draw conclusions. However, it was considered that the vast majority of wound infections had their origin in the operating theatre during the operation rather than in the wards. That opinion was based on the fact that when infection did occur, it was present at the first dressing, arising in the depths of the wound. The cause of the infection was a very complex problem. Dr. C. Kingston, assistant bacteriologist at Sydney Hospital in 1955, had made a detailed report on wound infection. Dr. Kingston had shown that faults could be observed in many stages of the aseptic procedures; infection could be due to unsatisfactory theatre design and ventilation, to out-moded sterilizers, to contaminated clothing worn by people in the theatre, or to breaches in aseptic technique by the operating team. Wound hæmatoma was thought to be a very important predisposing factor to infection. It was considered that surgeons who were most meticulous in controlling hæmorrhage had the lowest rate of wound infection. With regard to the organisms found on bacteriological analysis, *Staphylococcus pyogenes* was the most common. In 1954 it was present in 69% of infected wounds, in 1957 in 83%, and in 1958 in 71%.

DR. COLIN CONACHER asked Dr. Middleton whether, in the cases he had quoted from Oswestry and from the Royal North Shore Hospital, antibiotics had been used as a routine measure.

Dr. Middleton replied that antibiotics had not been used as a routine.

Dr. Conacher then referred to the fact that the routine parenteral use of antibiotics led to the development of resistant strains of organisms, and asked whether it was advisable to use antibiotics such as polybactrin and cicatrin locally in operation wounds.

Dr. Carruthers said that he considered it unwise to do so.

The other pathologists present disagreed with Dr. Carruthers. They considered that the risk that resistance would develop as the result of one application was very low indeed, and that the risk was even lower when more than one antibiotic was used.

Dr. Conacher then asked what were the anionic and cationic agents that antagonized each other.

The opinion was expressed that soap inactivated all other detergents.

Dr. Conacher finally asked whether occlusive dressings had any effect in reducing serious deep infections.

The answer was that they did not.

DR. P. M. ROUNTREE said that there had been much talk about the question of the infection rate and what was the best that could be achieved. She had some recent figures from St. Bartholomew's Hospital, from Sir James Paterson Ross, which suggested that under the best conditions there could be an infection rate of less than 1%. That would include all the types of wounds that had been discussed at the meeting, those that might have been infected in the wards and open wounds as well. At the Royal Infirmary in Bristol the figure was better—0·4%—so that in Australia they needed to set their house in order. They had certainly gone a step forward from the position when they had discussed the problem seven years previously. At least at the present meeting they had had figures from a number of hospitals, none of which did them any credit at all. Dr. Rountree said that it seemed to her that the actual essence of the problem had not yet been realized. The main factor appeared to be the staphylococcus, which was the cause of great trouble and was concerning people all over the world at the present time. To deal with it they had to realize that staphylococcal infection was an infectious disease; the patients were suffering from an infectious illness. Until such patients were nursed in that way, wound infections would occur. Staphylococci infected patients in the wards and started off infections in other patients; they might not necessarily do so directly, but they converted the members of the staff into nasal carriers, who could be responsible for transmitting the organisms into the surgical wards. The eradication of infection required a concerted effort on everyone's part. There should be isolation facilities for patients who contracted staphylococcal diseases in hospitals. Referring to the question of inefficient sterilization, Dr. Rountree suggested that people who thought they had inefficient sterilizers should observe how many infections with *Clostridia* they had. Dealing with the methods of use of antibiotics in the various hospitals, Dr. Rountree spoke first of what Dr. Carruthers had said about the use of penicillin and chloramphenicol. She asked whether he could give the incidence of resistant staphylococci at the Repatriation General Hospital, Concord. That would be very interesting to know, in the light of what they had been doing there over a long period. Referring to the topical application of antibiotics, Dr. Rountree said that most preparations made use of two antibiotics that were not employed in systemic therapy. The reason was that it was considered that the chance of getting a single resistant mutant in an organism responsive to one was not very great, but in one treated with two at once the chance of a doubly resistant mutant was extraordinarily small. So far nobody had been able to demonstrate a doubly resistant organism resulting from the use of those mixtures.

DR. JOHN SMYTH said that there was no difficulty in defining an infected surgical wound. Those wounds which had been sutured and exuded pus in any amount, no matter how small, were infected. That definition might leave out a few red wounds, but experience showed that most of those exuded pus later, and any error due to that was insignificant. Infected wounds must be counted by a doctor.

The surest way to deceive oneself into obtaining good figures was to have nurses do the recording and counting. The practice of keeping a "wound book" was to be deplored. The correct place for the state of the wound to be entered was on the patient's medical record. After all, the state of the wound was a significant part of his post-operative progress. Great difficulty would be encountered in ensuring that doctors entered the wounds, unless a surgical audit was made. The introduction of surgical audit solved that problem.

Dr. Smyth went on to say that since audit had been introduced for general surgery in Royal Newcastle Hospital, about 2500 wounds had been counted. The wound infection rates were much worse than those mentioned by other speakers, and averaged 15% for elective wounds and 30% for acute wounds. It was useless and misleading to speak of major and minor sepsis, and of "dirty" and "clean" operations. By counting only major sepsis after "clean" operations, it was possible to exclude bad results until good figures were obtained. That was very satisfying, but unlikely to introduce improvement. It might be mentioned in passing that after elective inguinal herniorrhaphy, when those strict criteria were used, the infection rate was 3%.

Dr. Smyth said that it was worth stressing again that the figures quoted were for general surgery. In the Royal Newcastle Hospital that excluded many traumatic procedures, as such patients were admitted under the accident service controlled by the orthopædic department. About 85% of general surgery in the hospital was abdominal. It was useless to compare general surgical and orthopædic wounds. The latter were always the better, but they had figures which threw doubt on the idea that "no-touch" technique was responsible, although at some 40% of operations one or more gloves were punctured. In fact, it was possible to divide general surgical wounds into two groups. In the one, containing such operations as thyroidectomy, mastectomy and elective hernia operations, the rate was comparable with the orthopædic rate. In the other, containing such operations as gastric, colonic and biliary tract procedures, the rate was very much higher, showing that the infected wound rate depended very greatly on the type of operation under discussion.

DR. ANGUS MCNEIL said that in 1957 he had been appointed to the B.M.A. committee, which had met about six times. It had gone through a great deal of literature, had called for reports from various hospitals, had run through films on the subject, and had considered the material available. The further the members of the committee went into the subject, the more frustrated they became. It was obvious that even with the most meticulous care there was an irreducible minimum of wound infection. They had come to the conclusion that apparently infection occurred mainly in the operating theatre; how it got into the wound nobody knew for sure. At the end of 1957 they had presented their preliminary conclusions to Professor Cruickshank, who was visiting Australia. Professor Cruickshank said that it was a most frustrating subject, and he could offer no real solution to the problem, other than to use common sense and the preventive principles that all knew were most important.

Medical Societies.

THE MEDICAL SCIENCES CLUB OF SOUTH AUSTRALIA.

A MEETING of the Medical Sciences Club of South Australia was held on December 5, 1958, at the Anatomy Department, University of Adelaide.

Lethal Jellyfish Stings: A Study in "Sea Wasps".

DR. R. V. SOUTHCOTT and DR. C. W. KINGSTON presented a study of the clinical, pathological and other aspects of lethal jellyfish stingings from Cubomedusæ, the "sea wasps" or "box jellies".

In introducing the subject, Dr. Southcott said that his attention had first been drawn to the subject 15 years earlier in North Queensland, when a number of cases of collapse and abdominal pain in swimmers had occurred. Two clinical types of stinging were differentiated, but difficulty occurred in establishing the identity of the stinging agents, and the difficulties had not yet been completely solved. That had led on to other aspects of the subject—taxonomy, toxicology and pathology. Deaths from jellyfish stingings occurred each summer in northern Australian waters, and further afield. Thus deaths had also occurred in the waters off New Guinea, Malaya, Borneo and the Philippines. In the past such deaths had been attributed by many authors to *Physalia*, the Portuguese man-of-war. However, a survey of the literature and requets through the medical Press had not disclosed a single documented death due to *Physalia* stinging. As far as present evidence allowed, most, or possibly all, deaths from acute jellyfish stingings were due to the Cubomedusæ. Small four-tentacled Cubomedusæ were found in temperate waters, where they caused stings with pain and vesiculation, and larger four-tentacled forms occurred in the tropics. The large many-tentacled Cubomedusæ were exclusively tropical. They reached maturity in the summer and autumn, when the bell might be the size of a pudding-basin, and the tentacles up to about 60 in number and several feet long. The Cubomedusæ occurred largely in inshore waters, over sandy bottoms, and preferred sheltered bays. They therefore preferred largely those conditions favoured by bathers. While much of the evidence that the Cubomedusæ were the lethal agents was circumstantial, there was some direct evidence. A jellyfish responsible for a fatality at Darwin in 1938 had been preserved, and was found to be a many-tentacled Cubomedusa, but on account of its mutilation and poor preservation, it had so far proved difficult to identify precisely. In northern Australian waters the Cubomedusa *Chironex fleckeri* Southcott 1956 was blamed for the fatalities, and in Philippine and other waters *Chiropsalmus quadrigatus* Haeckel 1879. At present the distribution of those forms was incompletely known, and the extent to which overlapping occurred was unknown. The Cubomedusæ were often difficult to see in the water, as they were practically transparent. After capture, the best general preservation was by the use of 5% to 10% formalin in sea-water, with care to prevent distortion and other damage.

Dr. Southcott went on to say that efforts were being made to study the toxins, which were injected by the nematocysts upon the tentacles. At present it was not known whether the lethal effect was due largely to the quantity of the venom available, or whether there were qualitative differences of significance occurring between the different Cubomedusæ. Nematocysts differed in type between the different Cubomedusæ. Nematocysts present along the weals of victims of fatal stingings matched those of *Chironex* and *Chiropsalmus* (*quadrigatus*). They did not match the nematocysts of other Cubomedusæ that had been studied. Such matching nematocysts were "banana-shaped" heteronemes and microbasic mastigophores. In general the principal stinging nematocysts of Cubomedusæ were microbasic mastigophores, but the "banana-forms" had been found only in *Chironex fleckeri* and *Chiropsalmus quadrigatus*. Nematocyst identification was therefore of medico-legal importance.

Studies on the physiology and toxicology of the venom of *Chironex* and other medusæ had been and were in progress. Dr. I. D. Hiscock was preparing for publication a paper on his studies on the physiological effects. Dr. S. Wiener, of the Commonwealth Serum Laboratories, had made some toxicological studies upon extracts of frozen tentacles sent by Dr. Hiscock. Dr. Wiener's findings, quoted by permission, were:

> Extracts of frozen tentacles [of *Chironex fleckeri*] were rapidly fatal to mice and guinea-pigs. Before death, paralysis of the hind-limbs was noticed; this was followed by coma with respiratory arrest. The heart continued to beat for several minutes after cessation of respiration. The internal organs of the guinea-pig showed intense congestion with hæmorrhages of the stomach and intestine. The intradermal injection into a guinea-pig caused local necrosis. In addition, a hæmolysin was present in the extract.
>
> All toxic principles including the hæmolysin were completely destroyed by boiling. This last observation suggests a protein structure of the toxic material.

Dr. Wiener had added a further note more recently, that as well as the report on *Chironex* that had been quoted, he had made some study of [*Catostylus*] *mosaicus*, identified by the Zoology Department, University of Queensland. The latter species preparation did not hæmolyse red cells to the same extent as *Chironex*, but was also toxic to mice. Antibodies produced against *Chironex* did not react with [*Catostylus*] *mosaicus*, so Dr. Wiener concluded that there was some specificity of antigens in medusæ.

Dr. Southcott then said that a further study of the toxins of *Chironex fleckeri* was at present being undertaken by Dr. J. Phillips, of the University of California. Dr. Phillips

had worked out a technique of preparing pure nematocyst suspensions from coelenterates by maceration in 1M sucrose solution and treatment in a Waring "Blendor", with differential centrifugation. By that method he had been able to obtain pure suspensions free from tissue extracts. At present tentacles of the Cubomedusæ were being removed from the living Cubomedusæ with scissors, and then placed immediately in pure glycerin. That was a new technique of Dr. Phillips, and it was hoped that it would provide an effective means of collecting and preserving venom.

Dr. Kingston discussed the histopathological features seen in the skin from two subjects dead of jellyfish stings from Queensland. One fatality had occurred at South Mission Beach, Tully, North Queensland, on December 13, 1957. The victim was a girl, aged 11 years. The other fatality had occurred at Townsville on December 13, 1956, the victim being an adult male, aged 38 years.

Dr. Kingston said that in standard skin preparations stained with hæmatoxylin and eosin, affected areas of skin showed swelling of the stratum corneum, shrinkage degeneration and pyknosis of the cells of the stratum Malpighii, and a number of circular to oval structures on the skin surface. When the light was considerably cut down by almost closing the condenser diaphragm, refractile threads could be seen penetrating through from the circular structures on the surface to the superficial dermis. The degenerative cellular changes were maximal in the presence of collections of these threads. Examination of frozen sections showed whole nematocysts on the surface of the skin, some unexploded, some partly exploded and some fully exploded with the threads penetrating the skin. They were found to be identical in size and shape with nematocysts similarly examined from Cubomedusan tentacles (*Chironex fleckeri* and *Chiropsalmus quadrigatus*).

Dr. Kingston finally said that after numerous staining techniques had been tried, a reticulum stain was found which impregnated nematocysts satisfactorily. Once again, identity of penetrating threads and surface vesicles with tentacle preparations was demonstrated.

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

THE MELBOURNE HOSPITAL.[1]

[From the *Australasian Medical Gazette*, March. 1883.]

There is much talk now about the necessity of removing the Melbourne Hospital to a more suitable site, not, of course, so much on account of the site as because the building requires reconstructing. There has been a large meeting of the contributors to discuss this question, and, like many other discussions, it has ended nowhere. The meeting adjourned for a month, and so, practically, the question is shelved. Perhaps there was some truth in the remarks of the Dean of Melbourne, that the public had acquired a sort of craze for pulling buildings down in order to put them up again: but, for all that, it cannot be denied that the Hospital is not wholly fit for its uses, either in respect of plan, arrangements, or materials, and that eventually it must be rebuilt either on its present or some other site. Traumatic erysipelas is never absent for very long from some of its wards, and it is not easy to escape the admission that the explanation is in the building itself. And of the Melbourne Hospital the resignation of the Medical Superintendent (Dr. Miller) has again raised the enquiry which preceded his appointment, two years ago, as to whether an experienced man with a large reputation should not be engaged at an adequate salary to take the general charge of this institution? It is easy to reply, off hand, to this query, but not so easy to reply satisfactorily. For if such a man as is really indicated were appointed, he could not well avoid coming in conflict with the honorary staff. In two conspicuous instances in this colony has a leading man taken charge of a large hospital, and, in both cases, the honorary staff became a negation. The resident superintendent grew to be the virtual dictator of the hospital: in one instance they resigned and left him master of the field, in the other they stood aside and occasionally were permitted to assist him. Altogether, therefore, I am not sure that the present arrangement at the Melbourne Hospital is not the best.

[1] From the original in the Mitchell Library, Sydney.

Correspondence.

A STOLEN OPHTHALMOSCOPE.

Sir: On the evening of Saturday, February 21, a Hamblin ophthalmoscope was stolen out of my car at Palm Beach.

If any medical practitioner or student is approached by any person wishing to sell an ophthalmoscope, would he or she please notify me or the police at once?

Yours, etc.,

R. A. Money.

"Harley",
143 Macquarie Street,
Sydney.
February 25, 1959.

DIAGNOSTIC RADIOLOGY.

Sir: In reply to Dr. Harris, I quite agree that few doctors would welcome one iota of increase in avoidable bureaucracy.

However, the small increase entailed by the registration of people operating lethal machines is inevitable, for the health of future generations can apparently not be entrusted to the conscience and common sense of the profession. (In spite of Dr. Stewart's work on leukæmia, I am still receiving requests to X ray women for "query pregnancy".)

Reassurances as to the smallness of the part played by diagnostic radiology in the over-all genetic hazard I believe to be useless. They are based on a false premise. Dr. Martin's figures on the amount of radiation received by patients X rayed under ideal conditions in a large city hospital cannot possibly apply to the amount received by the Australian public in general. This figure would be anybody's guess.

As to Dr. Harris's extraordinary attempt to compare her with that modern menace, the unskilled X-ray worker operating a long-exposure machine, I can just hear Miss Nightingale say: "Oh, leave these jargons, and go your way straight to God's work in simplicity and singleness of heart."[1]

Yours, etc.,

Mary Thornton.

Ringwood X-Ray Clinic,
15 Thanet Street,
Ringwood,
Victoria.
March 2, 1959.

TETANUS PROPHYLAXIS.

Sir: In common with all others engaged in general practice, I was intensely interested in the article on tetanus prophylaxis by Dr. Ackland (Med. J. Aust., February 7, 1959) and also in the other three references to the study of tetanus immunity in the same Journal.

This is a problem that concerns us all, and one that worries me a great deal at times—particularly the medico-legal aspect—and, I would like to make some observations of my own and put forward some questions which, I feel, need an authoritative reply.

I feel that the most difficult problem is that of recording injections. I agree that well-kept cards are ideal, but they are frequently unavailable when needed. In my own practice, of the last 50 children (under 12) that I have seen with some break in the skin's surface, 18 were not brought in by their parents, but by school teachers, neighbours or "hosts for the holidays". Of the remaining 32, in only 14 cases were the parents able to state that the child had been actively immunized or were the records available in my surgery; all the rest were doubtful as to what injections had been received or when. (Let us not hasten to condemn the parents of this last group. A very good friend and colleague

[1] Nightingale, Florence, "Notes on Nursing", Harrison, London.

of mine, a very capable general practitioner, when giving his latest child triple antigen, was unable to remember what injections he had given his first four children, so immunized them all again to make sure.)

Now, sir, what is my position with the first group of 18 children? Legally I cannot inject them without parental consent. If I go ahead with antitetanic serum and tetanus toxoid injections, am I liable for assault if, for instance, the parents object to injections? If I do not give the injections and tetanus supervenes, am I liable for negligence?

My personal method of dealing with children whose parents are not present is to give one c.cm. T.T. and to write a note to the parents informing them that if the child has not been immunized, then they should make arrangements for an ATS injection in 24 hours; I feel that the parents should assume some responsibility in the matter.

With regard to sensitivity testing, I feel that Dr. Ackland's recommendation is the counsel of perfection—well able to be carried out in hospital or in clinics during consulting or daylight hours, but rather difficult to carry out in the surgery late at night or at week-ends, owing to the amount of time involved. I suggest here that skin testing may be sufficient, and if any doubt arises, arrangements can be made for a subcutaneous sensitivity test to be made within 24 hours at a more convenient time and place.

Finally, sir, again on the question of recording immunity: would it not be possible to introduce some inert dyestuff or indian ink into the T.T., this coloured injection to be given in a universally agreed spot (e.g., six inches below the tip of the acromion) as the last of the series of T.T. injections? It should be possible to alter the dye strength so that it would be absorbed in a period of five years, so that if a strong spot of colour existed good immunity was likely, or a faded or dim spot visible, then a booster would suffice, or if no spot was seen, then a course of immunization would be necessary.

All my remarks, of course, refer to the minor or more trivial injuries, of which we in general practice see so many.

Yours, etc.,

DONALD CORDNER.

Tarawera,
Diamond Creek,
Victoria.
February 20, 1959.

THE JACKSON LECTURE: PROGRESS IN PSYCHIATRY.

SIR: Dr. G. B. Murphy, in his Jackson Lecture (MED. J. AUST., January 3, 1959), contented himself with a few petty criticisms of Freud's person. These, in my opinion (MED. J. AUST., January 17, 1959), bore little relevance to the significance of Freud's work to modern psychiatry. Dr. John F. Williams (MED. J. AUST., February 21, 1959) goes further. He "wonders" whether Freud's teachings regarding infantile sexuality and the Œdipus complex do not represent the delusions of a serene [sic!] paranoid! (And this, after reading *in toto* Ernest Jones's "Sigmund Freud: Life and Work"!)

Not being a psychiatrist, I can only wonder about the motives leading one to denigrate a man held in high regard throughout the world, even by those not entirely in agreement with him. Whether Freud's teachings are right will hardly be discovered in this type of correspondence. But human history abounds with examples of truths first enunciated by people with strange habits and peculiar backgrounds; and their more "normal" contemporaries, who branded them for being different, are long forgotten.

Yours, etc.,

A. M. LIEBHOLD.

65 Chapel Street,
St. Kilda,
Victoria.
February 25, 1959.

MEDICAL TECHNOLOGY CONVENTION.

SIR: I refer to Dr. Douglas's letter of February 21, 1959, headed "Medical Technology Convention", and heartily agree with him on the meaning of the word pathologist, and the rife but mostly unwitting misuse of that label on non-medical persons. However, I can see no objection to workers in medical laboratories being called medical technologists. Surely that name, though perhaps a little cumbersome, aptly describes a rather select group of people, who are trained for five years in the various branches of medical laboratory technique. They do a mighty job, on very poor pay, for patients by producing an accurate technical result which can be interpreted by a pathologist. There is no other group so trained to do this technical work, and for a pathologist to run a medical laboratory without technicians is like an artist trying to paint without a brush.

I agree with Dr. Douglas that it is desirable for all laboratories to be supervised by a specialist pathologist, but that is not always practicable. In these places the best substitute is a qualified medical technologist, who is trained to handle pathology specimens and, if necessary, give them the proper supervision "for transit to a pathologist". A qualified medical technologist can count cells, measure electrolytes and perform all laboratory techniques far better than the average practitioner. The latter would be the first to admit this. No worthwhile medical technologist assumes the role of a pathologist. We have to be practical on this subject and admit that many specimens and some pathologists do not travel well.

Dr. Douglas's dig at the "pecking order" of the visitors to the Medical Technology Convension is unkind. The programme was drawn up by an enthusiastic young man without ulterior motives who, with his colleagues, wished to raise the status of medical technology and to attract young people into this very worthwhile work. Their aim was achieved. Letters such as Dr. Douglas writes can only have the opposite effect.

Yours, etc.,

ALFRED GATENBY,
Pathologist.

Department of Pathology,
The St. George Hospital,
Kogarah, N.S.W.
February 24, 1959.

SIR: Having been associated with the education and training of medical laboratory workers in this State, throughout Australia, in New Guinea and the Fiji Islands, in both civilian life and the services over a period of many years, I feel qualified to say that the statements made by Dr. Douglas (MED. J. AUST., February 21, 1959) are incongruous and incorrect.

It is not my intention to indulge in "mud slinging", for I respect the practice of medicine and those responsible for its application, and I feel certain that the majority of pathologists and medical practitioners in Australia do appreciate the trained, experienced medical technologist, and will view the distasteful said communiqué with contempt.

Yours, etc.,

TERENCE J. WALDRON,
Diploma Examining Council in Medical Technology of New South Wales (appointed by the Hospitals Commission).

13 Kellett Street,
Kings Cross,
N.S.W.
February 25, 1959.

SIR: Dr. J. R. S. Douglas in THE MEDICAL JOURNAL OF AUSTRALIA, February 21, 1959, has drawn attention to the subject of technicians going beyond their proper duties, and his analogy of a doctor not expecting a theatre attendant to perform an operation is appropriate.

Irregular practices also occur in the radiographic field, and instances are known where radiographers have the habit of telling patients whether or not there is something wrong in the X ray, whereas this is the function of the doctor in charge of the patient.

Sometimes radiographers give interim reports upon films, and action may be based upon these interim reports which are unnecessary, as the doctor will see the X ray himself in the management of the patient.

Sometimes radiographers give reports upon the degree of union of fractures in patients who have had plaster removed and have been X rayed for progress. These reports by the radiographer may be given to an orderly untrained in physiotherapy, who will apply another plaster if the radiographer viewing the X ray recommends it. The patient's limb will not have been inspected by a medical officer before the new plaster is applied in many cases.

Occasions are known where orderlies, untrained in radiotherapy, take emergency X rays at nights and have given interim reports.

The performance of radiography is important, and there is more than enough for radiographers to do in their own field to ensure proper care and processing of films, proper radiographic exposures, and careful radiographic examination of patients with maximum protection of the patient's genes and other parts of the body. If these things fully occupied the attention of X-ray technicians, the community would be better off.

Now that Dr. Douglas has raised the question of "medical technologists" who are neither medical nor technologists, it would be interesting to hear his thoughts about technicians attending clinical meetings run by doctors.

Yours, etc.,

225 Dunbar Street,
Stockton,
N.S.W.
February 8, 1959.

Alan Grant.

Notes and News.

Proceedings of the Pan-Pacific Rehabilitation Conference.

The Pan-Pacific Rehabilitation Conference (International Society for the Welfare of Cripples) was held at Sydney on November 10 to 14, 1958. The Proceedings of the Conference are now being published. The subject matter covers all aspects of rehabilitation, from childhood handicaps to placement of handicapped persons in employment, and the papers presented are the work of experts in their field. Inquiries about this book should be directed to the Conference Secretary, Miss J. Garside, at the New South Wales Society for Crippled Children, 136 Chalmers Street, Sydney. The price of the book will be 30s.

Appointment of Director of Student Health Services, University of Sydney.

Dr. N. B. Malleson has been appointed to the recently created position of Director of the Student Health Service, University of Sydney. Dr. Malleson holds the degrees of master of arts, bachelor of medicine and bachelor of surgery of the University of Cambridge, and is a member of the Royal College of Physicians of London. He served with the Royal Air Force Volunteer Reserve in the United Kingdom and in India, and has had considerable experience in various spheres of medical practice. He held a senior Fulbright research scholarship and worked at the University of Michigan during 1952, and in 1954 visited the U.S.S.R. as a member of a medical delegation. In 1956 he attended an international conference on student mental health at Princeton, U.S.A. Since 1949 he has been physician in charge of the Student Health Service at University College, London. Dr. Malleson is regarded as a leading authority on student health services.

Post-Graduate Work.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

General Revision Course, May 11 to 22, 1959.

The Post-Graduate Committee in Medicine in the University of Sydney announces that the annual general revision course will be held in Sydney for two weeks beginning May 11, 1959. As in the previous courses, the main emphasis is on therapeutics, and in addition the programme, as in former years, is a comprehensive survey of modern trends in diagnosis and treatment of special value to general practitioners. The programme is as follows:

Monday, May 11, in the Stawell Hall, 145 Macquarie Street, Sydney: 9.15 a.m., registration; 9.45 p.m., welcome and opening of course; 10 a.m., review of course; 10.45 a.m., "Medical Aspects of Air Travel", Dr. E. H. Anderson; 11.45 a.m., "Control and Treatment of Staphylococcal Infections", Sir William Morrow; 2 p.m., symposium on "Hypertension", Professor C. R. B. Blackburn in the chair; 2 p.m., "Diagnosis and the Importance of the Kidneys", Professor C. R. B. Blackburn; 2.20 p.m., "The Use of Chlorothiazide", Dr. R. B. Blacket; 2.40 p.m., "Management of the Patient", Dr. F. L. Ritchie; other lecturers yet to be decided.

Tuesday, May 12, in the Stawell Hall, 145 Macquarie Street, Sydney: 9.15 a.m., symposium on "Common Skin Diseases in General Practice", Dr. R. B. Perkins in the chair; 9.15 a.m., "The Management of Skin Cancer in General Practice", Dr. J. C. Belisario; 9.35 a.m., "Recurrent Boils", Dr. W. K. Myers; 9.55 a.m., "Therapeutic Hints", Dr. A. G. Finley; 10.35 a.m., "Acne", Dr. E. Murray-Will; 10.55 a.m., "Emotional Factors in Neuro-Dermatitis", Dr. E. J. C. Molesworth; 11.15 a.m., discussion; 11.35 a.m., group photograph of members; 11.55 a.m., "Collagen Diseases", Dr. Ralph Reader; 2.15 p.m., "Radiation in Medical Practice", Dr. L. A. Atkinson and Dr. E. P. George; 3.45 p.m., "Civil Defence", Major-General I. N. Dougherty, D.C.D.

Wednesday, May 13, in the Stawell Hall, 145 Macquarie Street, Sydney: 9.15 a.m., "Diagnosis of Difficult Cases of Diarrhœa", Dr. Stanley Goulston; 10.45 a.m., "Cancer Detection in General Practice", Dr. Keith Jones; 11.45 a.m., "Fractures Around the Elbow Joint", Dr. F. H. McC. Callow; afternoon, free; film screenings to be arranged by Dr. F. A. Bellingham; 8.15 p.m., symposium, "What's New in Drugs and Therapeutics", Dr. C. G. McDonald in the chair; 8.15 p.m., "Intelligent Hormone Therapy in Obstetrics and Gynæcology", Professor B. T. Mayes; 8.35 p.m., "Treatment of Diabetes", Dr. W. Wilson Ingram; 8.55 p.m., "Treatment of Electrolyte Disturbances in Medical Crises", Dr. J. E. Hassall; 9.15 p.m., question time.

Thursday, May 14: Stawell Hall, 145 Macquarie Street, Sydney: 9.15 a.m., "Parkinson's Disease" (with film), Dr. George Selby and Dr. J. M. F. Grant; 10.45 a.m., "A Review of Some Common Respiratory Diseases", Dr. H. Maynard Rennie; 11.45 a.m., "Poisoning in the Home", Dr. Clair Isbister. Broughton Hall Psychiatric Clinic, Leichhardt: 2.15 p.m., demonstration of psychiatric problems by Professor W. H. Trethowan and the staff. Stawell Hall, 145 Macquarie Street: 8.15 p.m., "Modern Trends in First Aid", Mr. W. Gissane, F.R.C.S. (England and Edinburgh), Surgeon-in-Chief, Birmingham Accident Hospital.

Friday, May 15, in the Stawell Hall, 145 Macquarie Street: 9.15 a.m., panel discussion on "Problems in Medical Practice"; moderator, Dr. V. M. Coppleson; specialist panel, Dr. Selwyn Nelson, Dr. R. H. Macdonald, Dr. P. J. Kenny; course panel—six members of the course will be chosen to act as monitors.

Saturday, May 16, at the Red Cross Blood Transfusion Centre, 1 York Street, Sydney: 9.15 a.m., demontrations of blood grouping, Rh testing and blood transfusion techniques, Dr. Hugh K. Ward and Dr. R. J. Walsh.

Monday, May 18, in the Stawell Hall, 145 Macquarie Street: 9.15 a.m., symposium on "The Multi-Discipline Approach to the Maternity Case", Professor Bruce T. Mayes in the chair: 9.15 a.m., "Some Recent Advances in Hormone Therapy", Dr. Rodney Shearman; 10 a.m., "Infant Welfare in the First Six Months of Life, Including Reference to Neonatal Anoxia", Dr. Wilfred Cary; 11.15 a.m., "Social Aspects of Obstetrics", Miss Lorna D. Nolan; 12 noon, question time; 2 p.m., symposium on "Gynæcological Problems in General Practice", Dr. George Stening in the chair; 2 p.m., "What Can You Do for the Infertile Couple (Male)?", Dr. Derby Loudon; 2.15 p.m., "What Can You Do for the Infertile Couple (Female)?", Dr. W. G. Jasper; 2.40 p.m., discussion; 3 p.m., "Management of Abortion", Dr. G. M. Parkin; 4.30 p.m., "Ovarian Malignancies", Dr. A. R. H. Duggan.

Tuesday, May 19, in the Main Lecture Theatre, Royal Alexandra Hospital for Children, Camperdown: 9.15 a.m., "The Investigation of the Infant who Fails to Thrive", Dr. Kathleen Winning; 10.30 a.m., "Neonatal Jaundice", Dr. A. R. Tink; 11.30 a.m., "Abdominal Pain in Childhood", Dr. E. S. Stuckey and Dr. C. A. Rigg; 2.15 p.m., "Management of Burns in Childhood", Dr. A. W. Middleton and Dr. W. Grigor; 3.30 p.m., "Gamma Globulins and Sera in Pædiatric Practice", Dr. John Beveridge; 4.30 p.m., question time, Dr. S. E. J. Robertson, Dr. A. W. Middleton and Dr. John Beveridge.

Tuesday, May 19, in the Stawell Hall, 145 Macquarie Street: 8.15 p.m., "Acute Myocardial Infarction and its Treatment", Dr. Rae Gilchrist, F.R.C.P., Physician to the Royal Infirmary, Edinburgh, and President of Royal College of Physicians, Edinburgh.

Wednesday, May 20, in the Stawell Hall, 145 Macquarie Street: 9.15 a.m., "Ophthalmology in General Practice", Dr. K. B. Armstrong; 10.45 a.m., "Anæsthesia in General Practice", Dr. W. I. T. Hotten; 11.45 a.m., "Urology in General Practice", Dr. Colin Edwards; 2.15 p.m., "Ear, Nose and Throat in General Practice", Dr. George Halliday; 3.45 p.m., "Pathology for the General Practitioner", Dr. G. V. Rudd.

Thursday, May 21, in the Stawell Hall, 145 Macquarie Street: 9.15 a.m., electrocardiographic demonstration, Dr.

G. E. Bauer; 10.45 a.m., "A Physician's Approach to Back and Neck Pain", Dr. Selwyn Nelson; 11.45 a.m., "Treatment of a Few Common Allergic Diseases", Dr. Bernard Riley; 2.15 p.m., symposium on "Recognition and Management of Emergencies in Post-Operative Care", Professor John Loewenthal in the chair; 2.15 p.m., "Post-Operative Shock and Hæmorrhage", Dr. Denis Arnold; 2.35 p.m., "Thromboembolism", Dr. D. C. Mackenzie; 2.55 p.m., "Pulmonary Atelectasis and Pneumonitis", Dr. W. I. T. Hotten; 3.15 p.m., "Fluids, Electrolytes and the Hormonal Response", Dr. J. P. Halliday; 4.05 p.m., "Mechanical and Adynamic Obstruction", Dr. G. W. Milton; 4.25 p.m., "Peritonitis and Residual Abscesses", Dr. David Glenn; 4.45 p.m., "Wound Infection and Dehiscence", Dr. R. Gye.

Friday, May 22, in the Stawell Hall, 145 Macquarie Street: 9.15 a.m., panel discussion on "Problems in Medical Practice"; moderator, Dr. V. M. Coppleson; specialist panel, Professor Bruce T. Mayes, Professor John Loewenthal, Professor W. H. Trethowan; course panel—six members of the course will be chosen to act as monitors; 11.30 a.m., discussion groups; 12.30 p.m., conclusion of course.

Social Activities.

Social activities arranged during the course include a cocktail party at the Hotel Australia on Tuesday, May 12, at 5.30 p.m.

The Post-Graduate Golf Cup competition will be played at the Royal Sydney Golf Club, Rose Bay, on Friday, May 15, from 12.30 p.m. The Brydon cup will be awarded to the country member attending the general revision course who obtains the best score.

Post-Graduate Oration, 1959.

In the presence of His Excellency the Governor of New South Wales, the twelfth annual Post-Graduate Oration will be given by Professor A. A. Abbie on "Sir Grafton Elliot Smith" on Wednesday, May 20, 1959, at 8.15 p.m., in the Great Hall of the University of Sydney.

Fees and Method of Enrolment.

Fees for attendance are: Full course, £12 12s.; morning or afternoons only, £6 6s.; one week only, £6 6s. Early application, enclosing remittance, should be made to the Course Secretary, The Post-Graduate Committee in Medicine, 131 Macquarie Street, Sydney. Telephones: BU 4497-8. Telegraphic address: "Postgrad Sydney."

Fees and travelling expenses for this course are taxation deductions. When such deductions are claimed, "Taxation—File No. AF/1865" should be quoted.

Course in the Care of Handicapped Children at Newcastle.

Dr. L. T. Hilliard, M.B., B.Ch., M.R.C.S., D.P.M. (England), who is Consultant Psychiatrist and Physician Superintendent at the Fountain Hospital, London, and an expert in the management of subnormal and physically handicapped children, will conduct a course on "Recent Advances in Mental Deficiency and Care of Physically Handicapped Children", which will include visits to various mental institutions in the area. The course will begin with an evening lecture on Monday, April 13, 1959, and will conclude with a demonstration at Watt Street Hospital on Thursday morning, April 16. No fees will be charged to members of the annual subscription course, or to D.P.M. II candidates. The fee for non-members is £2 2s. The course is limited to 20 selected candidates, preference being given to those who are actively engaged in work in this field. A few vacancies still remain. Those wishing to apply should communicate by April 3 with the Course Secretary, The Post-Graduate Committee in Medicine, 131 Macquarie Street, Sydney. Telephones: BU 4497-8.

Annual Subscription Course.

Dr. L. T. Hilliard, M.B., B.Ch., M.R.C.S., D.P.M. (England), Consultant Psychiatrist and Physician Superintendent, the Fountain Hospital, London, will give the following lectures in the annual subscription course: Wednesday, April 8, at 8.15 p.m., in the Stawell Hall, 145 Macquarie Street, Sydney: "Community Care of the Feeble-Minded" (in conjunction with the N.S.W. Association for Mental Health). Thursday, April 9, at 9.30 a.m., at the Child Guidance Centre, Brisbane Street, Sydney: "Problems of Mentally Deficient Children". (There are a limited number of places available for medical practitioners, and those desirous of attending should 'phone Dr. Beryl Cooley, LA 5327.) Thursday, April 9, at 2.30 p.m.,

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED FEBRUARY 21, 1959.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	1	3(3)	1(1)	..	..	..	..	..	5
Amœbiasis	..	..	..	..	..	..	1	..	1
Ancylostomiasis	..	..	..	..	..	..	10	..	10
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	..	..	..	..	..	..	..	..
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	6(2)	8(7)	2	..	..	..	..	1	17
Diphtheria	1	..	..	5(1)	..	..	..	..	6
Dysentery (Bacillary)	..	8(2)	1(1)	2(2)	1(1)	..	2	1	15
Encephalitis	..	..	..	..	..	..	..	..	..
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	75(22)	45(38)	15(10)	7(6)	6(6)	..	5	2	155
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	1	..	..	1	..	1	..	3
Leptospirosis	1	..	..	..	..	..	..	..	1
Malaria	..	..	5(3)	..	..	..	..	..	5
Meningococcal Infection	..	1	..	..	..	..	..	..	1
Ophthalmia	..	..	..	..	1	..	..	..	1
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	2(2)	..	..	..	..	..	..	..	2
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	..	..	..	..	..	..	..	..	..
Puerperal Fever	1	..	..	..	..	..	..	..	1
Rubella	..	20(17)	..	1	9(9)	..	1	..	31
Salmonella Infection	..	..	..	3(3)	..	..	..	..	3
Scarlet Fever	5(1)	11(9)	1	..	1(1)	..	..	..	18
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	..	1	..	..	..	..	1
Trachoma	..	..	..	..	66	..	10	..	76
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	19(14)	16(11)	13(6)	14(12)	7(6)	7(1)	..	..	76
Typhoid Fever	..	..	..	..	..	..	..	..	..
Typhus (Flea-, Mite- and Tick-borne)	..	..	..	..	..	..	..	..	..
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

at Broughton Hall Psychiatric Clinic, Wharf Road, Leichhardt: "A New Approach to the Problems of Mental Subnormality." Monday, April 13, at 8 p.m., at The Royal Newcastle Hospital: "Recent Research into Mental Deficiency." Wednesday, April 22, at 11 a.m., at the Institute of Child Health, Royal Alexandra Hospital for Children: "A New Approach to the Problems of Mental Subnormality." Thursday, April 23, at 8.15 p.m., at the Robert H. Todd Assembly Hall, 135 Macquarie Street, Sydney: "Recent Research into Mental Deficiency" (in conjunction with the Australian Association of Psychiatrists).

Dr. Hilliard's visit has been sponsored by the Post-Graduate Medical Foundation, the Watt Street Hospital Handicapped Children's Welfare Association and the Government of New South Wales, through the Post-Graduate Committee in Medicine in the University of Sydney.

SEMINARS AT THE WOMEN'S HOSPITAL, CROWN STREET, SYDNEY.

Owing to the close proximity of Easter to the first Wednesday of April, the seminar at the Women's Hospital, Crown Street, Sydney, will be held on April 8 instead of April 1.

Nominations and Elections.

The undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Szekulesz, Istvan, M.D., 1950 (Univ. Budapest) (registered in accordance with the provisions of Section 17 (2A) of the *Medical Practitioners Act*, 1938-1958), 93 Old South Head Road, Bondi Junction.

Cook, Peter, M.B., B.S., 1953 (Univ. London), D.R.C.O.G., 1956, 143 Woodland Street, Balgowlah.

Levi, Louis, M.B., B.S., 1955 (Univ. Sydney), 183 Macquarie Street, Sydney.

Hollo, Stephen Julian, M.D., 1950 (Univ. Budapest) (registered in accordance with the provisions of Section 17 (2A) of the *Medical Practitioners Act*, 1938-1958), 18 Paul Street, Balmain.

The undermentioned have been elected as members of the New South Wales Branch of the British Medical Association and have been provisionally registered with the qualifications of M.B., B.S., 1959 (Univ. Sydney), unless otherwise stated: Allardyce, Clive Frazer; Baume, Peter Erne; Finlayson, Paul Farrington; Ogborne, Warren Lambert; Storey, Brian Gilbert; Aroney, Charles James, M.B., B.S., 1957 (Univ. Sydney); Grainger, Peter Francis, M.B., B.S., 1956 (Univ. Sydney); Hugh, Thomas Benedict, M.B., B.S., 1957 (Univ. Sydney); Learoyd, Brian Meldrum, M.B., B.S., 1955 (Univ. Sydney); Leber, Carl Frederick, M.B., B.S., 1956 (Univ. Sydney); Lynch, John Michael Joseph, M.B., B.S., 1957; McCullough, Russell Hugh, M.B., B.S., 1952 (Univ. Sydney); McDonald, Barry John, M.B., B.S., 1957 (Univ. Sydney); Sutherland, Donald Fyfe, M.B., B.S., 1956 (Univ. Sydney); Teo, Philip Seng Kee, M.B., B.S., 1957 (Univ. Sydney); Wallner, Darrell Peter, M.B., B.S., 1957 (Univ. Sydney).

Medical Appointments.

Dr. R. J. Smith has been appointed Government Medical Officer at Surat, Queensland.

The undermentioned have been appointed members of the Advisory Committee of the Royal Adelaide Hospital, Adelaide: Dr. I. B. Jose (nominated by the Council of the University of Adelaide), Dr. K. S. Hetzel (nominated by the Faculty of Medicine of the University of Adelaide), Sir Brian H. Swift (nominated by the Board of Management of the Royal Adelaide Hospital), Dr. R. M. Glynn (nominated by the Board of Management of the Royal Adelaide Hospital), Dr. A. H. Lendon (nominated by the honorary medical staff of the Royal Adelaide Hospital), Dr. M. E. Chinner (nominated by the honorary medical staff of the Royal Adelaide Hospital), Dr. J. E. Hughes (nominated by the Royal Australasian College of Surgeons), Dr. C. B. Sangster (nominated by the Royal Australasian College of Physicians).

Deaths.

The following death has been announced:

Curzon.—Maurice Curzon, on March 13, 1959, at Melbourne.

Diary for the Month.

April 1.—Western Australian Branch, B.M.A.: Branch Council.
April 1.—Victorian Branch, B.M.A.: Branch Meeting.
April 2.—South Australian Branch, B.M.A.: Council Meeting.
April 3.—Queensland Branch, B.M.A.: General Meeting.
April 7.—New South Wales Branch, B.M.A.: Organization and Science Committee.

Medical Appointments: Important Notice.

Medical practitioners are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales. Anti-Tuberculosis Association of New South Wales.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Editorial Notices.

All articles submitted for publication in this Journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations, other than those normally used by the Journal, and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of the article. The abbreviations used for the titles of journals are those of the list known as "World Medical Periodicals" (published by the World Medical Association). If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors submitting illustrations are asked, if possible, to provide the originals (not photographic copies) of line drawings, graphs and diagrams, and prints from the original negatives of photomicrographs. Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

Original articles forwarded for publication are understood to be offered to The Medical Journal of Australia alone, unless the contrary is stated.

All communications should be addressed to the Editor, The Medical Journal of Australia, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2-3.)

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